Optimal configuration and planning of a blood supply chain network under an uncertain environment

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Abstract
Blood products are indispensable to life. Besides, they are perishable and there are no substitutes. Supply depends on voluntary donations and is therefore irregular over time, and demand is stochastic, depending in part on unpredictable events. Given the vital nature of blood products, shortage scenarios are not acceptable and wastage is also ethically reprehensible since human blood is obtained through the solidarity of donors. It follows, then, that the management of the blood supply chain is complex. The aim of this study is to understand how the blood supply chain has been studied and how is possible to contribute to the optimal design of such system considering uncertainty. Thus, a comprehensive tactical-strategic optimisation model is developed that allows studying the optimal planning and location of blood facilities. The model addresses uncertainty by means of two-stage stochastic programming and minimises operational costs inherent to supply chain operation, wastage, shortages, substitutability and carbon emissions. In addition, a case study of the Portuguese blood supply chain is presented. The panorama of activity in the blood domain in Portugal reveals wastage and a recurrent imbalance between demand and supply. The model developed is applied to the particular case of the Lisboa e Vale do Tejo region considering the deterministic and stochastic developed approaches. It is concluded that the stochastic approach presents lower wastage, compared to the deterministic one, but higher shortage and, consequently, lower service level.
Keywords: Blood Supply Chain; Network Design; Perishability; Two-Stage Stochastic Programming; Uncertainty.

1. INTRODUCTION

The first successful blood transfusion (an operation by which blood or specific blood components from one organism are passed into the circulatory system of another) took place in 1818. However, severe reactions in transfused patients were usual, resulting in many deaths. In 1900, Karl Landsteiner took one of the most valuable steps in blood research by discovering the existence of three blood types – A, B and O. Two years later, another blood type was discovered, AB, thus completing the ABO system (National Blood Transfusion Service, 2020). Despite the knowledge of the ABO system and the compatibility relationships between the different blood types, serious reactions continued to occur as a result of transfusions. It was in 1939 that another blood system was discovered – the Rhesus (Rh) system, whereby blood can be further classified as Rh positive (+) or Rh negative (–). This concluded the discovery of the most commonly used blood classification, ABO/Rh, which results in eight blood types: A+, A–, B+, B–, AB+, AB–, O+ and O– (American Red Cross, 2021). It is now known that blood plays a very important role in breathing, nutrition, regulation and defence of the human body. It is mostly made up of red blood cells (RBCs), white blood cells and platelets (PLTs), immersed in a liquid called plasma (Etablissement Français du Sang, 2021). Despite scientific and technological progress in recent decades, disparities in the blood supply between developed and developing countries still exist. According to the World Health Organization (2021), 40% of the world's total donations are collected in developed countries, home to only 16% of the world's population. The donation rate in developing countries is only five donations per 1,000 inhabitants, which compares to 31.5 donations per 1,000 inhabitants in developed countries. In the latter, blood products are used to support advanced medical procedures such as surgery or cancer treatments. Blood products are defined as whole blood (WB), i.e., blood in its unaltered state after collection, and WB-derived products. The most common of these are RBC and PLT concentrates, and plasma. The establishment of several blood facilities, constituent parts of the blood supply chain (BSC), is essential to ensure the collection, production, storage and distribution of safe, effective and quality blood products. The World Health Organization (2021) recommends that blood facilities should be coordinated at a national level,

establishing integrated networks of blood supply. For these blood facilities to fulfil their primary mission, which is matching supply with demand, they must be strategically designed. Supply chain network design (SCND) consists of planning the physical location and capacity of facilities and aims to find the most efficient network configuration. Thus, it must consider several parameters, such as costs and distances, and the specifics of the products. Blood is perishable, i.e., it has a very limited shelf life after which it must be discarded (Nagurney et al., 2012). There is also a wide range of blood types and products that require specific storage and transport conditions. Moreover, no blood product has substitutes and their availability depends on the solidarity of voluntary unpaid donors (World Health Organization, 2010). It follows that supply is fairly irregular over time, constituting a source of uncertainty, alongside demand, which is also stochastic (Nagurney et al., 2012). As blood products are vital, it is not acceptable that they are not available when needed, but their wastage is also reprehensible. All these factors make the design of BSC networks highly complex and research-worthy. The objective of this paper is to develop a more comprehensive mathematical optimisation model in the context of SCND under supply and demand uncertainty, given the existing literature. The model is then applied with the Portuguese context as a case study.

The remaining paper is organised as follows: Section 2 presents the literature review; Section 3 presents the mathematical formulation of the optimisation model developed; Section 4 presents the case study; Section 5 presents the results and discussion; and Section 6 presents the main findings, concluding the paper.

2. LITERATURE REVIEW

There are several reviews on the BSC, two of which stand out. Osorio et al. (2015) develop their review on quantitative models in the BSC and organise them into five categories. The first four focus on each of the echelons of the BSC – Collection, Production, Inventory and Distribution. The fifth category presents models that integrate all the echelons. The authors conclude that most literature focuses on only one echelon and thus there is a significant gap regarding models that integrate the entire BSC flow. Pirabán et al. (2019) published a review in which the existing work is assigned to five categories – decision-making and forecasting environments, issues in the design of the BSC, processes and problems/planning decisions, modelling and solution methods, and data characteristics. The authors conclude that one of the main gaps in the literature relates to complex BSC configurations that consider several echelons and several facilities, and that study the interactions between them under an uncertain environment. There are mainly two types of BSC configurations – centralised and decentralised systems (Beliën & Forcé, 2012; Osorio et al., 2015). Decentralised systems are characterised by many dedicated blood facilities. Each of these facilities is independent, so they have the autonomy to govern themselves and decide on their operating policies. These systems are more common in developing countries. Centralised systems, in turn, consist of several regional divisions, these having one or more blood facilities. Administration and authority over decision-making lie with top management that sets out the procedures to be followed by these facilities. Thus, the blood facilities act in a coordinated manner and are interdependent. These systems predominate in developed countries and one of the main drivers of centralisation is economies of scale, allowing significant cost savings (Osorio, Brailsford, Smith, et al., 2018). Hence, it is the centralised systems that are focused on in this paper.

BSC Echelons

Collection is the first echelon in the BSC and aims to obtain the quantity of blood needed to satisfy the demand for blood products (Pirabán et al., 2019). It can be performed by two methods – WB collection and apheresis. The former consists of a blood withdrawal with the same composition as that circulating in the donor (Özener et al., 2019). Apheresis consists in collecting isolated blood components. As such, it requires specialised equipment to extract only the desired components and return the remaining blood to the donor (Instituto Português de Oncologia do Porto Francisco Gentil, 2020). Collection sessions take place in dedicated locations such as blood centres (BCs), hospital blood units, mobile venues, and bloodmobiles. BCs and hospital blood units, referred to as fixed collection sites, are fixed facilities permanently equipped for collection. Bloodmobiles are dedicated blood collection vehicles also permanently equipped that travel to various sites (DOMAINE, 2010). Mobile venues, in turn, refer to collection sessions organised in facilities that are not permanently equipped. Thus, bloodmobiles and mobile venues are referred to as temporary collection sites since they can be moved between several geographic points over time. Contrarily, the location of fixed collection sites is defined in the long term, so it cannot be changed during the planning horizon (Gunpinar & Centeno, 2016; Zahiri et al., 2013). Lowalekar & Ravichandran (2010) consider that the quantity of blood to be collected can be restricted to reduce wastage stemming from over-collection scenarios. The authors analyse three policies – unrestricted

collection, which consists of collecting blood from all donors, Modified (Q, T) and Modified (R, T). Modified (Q, T) consists of collecting a fixed quantity of blood Q, and Modified (R, T) of collecting a quantity that is equal to the difference between a target inventory level R and the stock level immediately before collection. Their conclusions demonstrate that the latter two outperform unrestricted collection in controlling total costs and wastage. After collection, the production echelon follows. This includes the testing and processing of blood components. Testing should ensure the quality, compatibility, and safety of blood and takes place at laboratories that are typically located within BCs (Nagurney et al., 2012; Pirabán et al., 2019). Fragoulakis et al. (2014) appraise the production cost of a blood unit in Greece. The study considers the resources spent in the collection, testing, processing and storage processes, and also the indirect cost of blood donations for donors, i.e., the productivity loss. The authors conclude that the cost of testing is very significant, representing 55.62% of the total cost of obtaining a unit of blood. At the same time as a fraction of the donations are tested, the remaining blood proceeds to the processing centres, which are also typically located within the BCs. Processing consists of using a centrifuge machine to separate blood components according to their density. This process is called fractionation and, depending on the speed and time of centrifugation, different blood products are obtained (Osorio, Brailsford, & Smith, 2018). Although fractionation allows only the desired blood products to be produced, i.e. it allows to adapt production to the needs of patients, it may not always be optimal to fractionate large amounts of WB, since the increased availability of blood products might also imply an increase in the costs of holding, processing and wastage in the BC (Beliën & Forcé, 2012; Lowalekar & Ravichandran, 2011). In this regard, Lowalekar & Ravichandran (2011) develop a simulation-based model to determine the optimal amount of WB to be fractionated in a BC. Their work proves to be an important contribution to the management of BCs, as it presents a tool that allows testing the impact that processing different amounts of WB has on the overall performance of the BC. The inventory echelon comprises the storage and inventory management processes. Storage consists of properly preserving blood products, i.e., according to their storage conditions. It takes place at BCs and hospital blood banks, these being intended for pre-transfusion storage. Inventory management refers to a set of policies aimed at ensuring the availability of blood in sufficient quantity to meet demand. According to Duan & Liao (2014) and Osorio et al. (2017), the most commonly used inventory review policy in BCs is a 1-day period, meaning that the inventory state is updated every day. The 1-day period review policy is particularly advantageous as it allows for the coordination of inventory replenishment with distribution, which often occurs daily. As per Osorio et al. (2017), demand nodes review their inventory level daily, following an order-up-to-level (R, S) policy. When the observed inventory level of a blood product is lower than a certain value, a replenishment order is placed to increase the inventory back up to the S level. Also, there are two issuing policies frequently addressed in the literature – First In, First Out, in which the products despatched are those that have been stored the longest, and Last In, First Out, in which the products despatched are the ones that have been stored most recently (Pirabán et al., 2019). At BCs, orders are usually issued according to First In, First Out policy and processed in batches according to the average daily demand of the demand nodes served by the BC (Blake et al., 2013). Distribution refers to the movement of blood products between facilities in the BSC and it covers two processes – shipment and distribution to demand nodes. Shipment takes place immediately after collection and consists of transporting blood collections from temporary collection sites to blood BCs, as WB must be processed within six hours after collection (Özener & Ekici, 2018; Pirabán et al., 2019). Şahinyazan et al. (2015) suggest the usage of motor vehicles, called shuttles, which would visit all bloodmobiles and transport the collected blood to the BCs. Shuttles would also be able to provide the bloodmobiles with additional collection material resources when needed so that bloodmobiles would not have to return to the BC every day (Pirabán et al., 2019). As regards distribution to demand nodes, blood products in demand are transported from the BCs by vehicle fleets that must ensure timely delivery. Blood products may also be transported between facilities, whether these BCs or demand nodes, when there are shortages in one location and over-supply in another (Osorio et al., 2015). This is called lateral transhipment and two types exist – proactive and reactive transhipment. The former one occurs at predetermined moments in time before demand is realised. The latter one occurs when an inventory shortage is realised and acts as a quick and effective solution to relieve the supply pressure of the demand nodes (Dehghani et al., 2021; Paterson et al., 2011).

Supply chain network design

SCND is one of the most important activities in supply chain management as it determines the physical configuration of the network, i.e., the quantity, type, location and physical characteristics of the facilities, such as capacity.

This is a problem that stems from a set of strategic planning decisions associated with large initial investment values, and it is generally not possible to change the network configuration in the short term (Govindan et al., 2017). In this sense, the network design of the supply chain (SC) is determinant both in the definition of the cost structure, and consequently in the profitability, as well as in the performance of the SCs. According to Govindan et al. (2017), most work on the topic addresses single-period decisions, i.e., decisions considering only one time horizon, and relating to facilities of one or two echelons. Given that SCND concerns long-term decisions, it is important to note that the most common parameters are not deterministic, changing over time (Moreno-Camacho et al., 2019). As such, the decision-making environment is rather complex and uncertain. Indeed, uncertainty emerges as a key planning factor and several recently published research papers consider it. SCND problems under uncertainty aim to configure networks that ensure the regular performance of SCs whatever the environment in which they are inserted, and there are different quantitative approaches to address them (Govindan et al., 2017). According to Tordecilla et al. (2021), these are mainly divided into optimisation and simulation. The authors observe that the use of optimisation is more popular than simulation since the latter does not allow obtaining optimal or near-optimal solutions. With regard to mathematical approaches to modelling optimisation problems, the most popular are stochastic programming, robust optimisation, and fuzzy programming. Stochastic programming is suited for decision-making environments in which the probability distributions of uncertain parameters are known and the most common approach is scenario-based. Scenario-based stochastic programming is subdivided into two approaches – two-stage stochastic programming and multi-stage stochastic programming. According to Govindan et al. (2017), two-stage stochastic programming is the most widespread approach. The first stage corresponds to decision-making at the strategic planning level, such as the location of facilities and their capacity, and takes place before the realisation of the uncertain parameters; the second stage corresponds to decision-making at the tactical and operational planning level. Multi-stage stochastic programming applies to situations in which decisions must be non-anticipative, i.e., they must not depend on the future values of uncertain parameters. Robust optimisation is used in decision-making environments where there is little or no access to historical data and it is not possible to estimate the probability distributions of uncertain parameters (Heidari-Fathian & Pasandideh, 2018). Robust optimisation is particularly relevant in developing worst-case optimisation models of SC network performance. Fuzzy programming applies to decision-making environments whose uncertainty is non-probabilistic. There are two approaches – flexible programming and possibilistic programming (Eskandari-Khanghahi et al., 2018). The former assumes that the values of uncertain parameters are set by the decision-makers, so they are subjective (Jafarian et al., 2018). In the latter, the uncertain parameters values and the formulation of the model constraints are based on available quantitative data and the qualitative insights of the decision-makers (Eskandari-Khanghahi et al., 2018). In addition to mathematical approaches, it is important to introduce solving approaches. Among these are the exact methods and metaheuristics (Tordecilla et al., 2021). The main difference between these is that exact methods guarantee that optimal solutions are obtained for the optimisation problems, which is not the case for metaheuristics. The computational execution of these problems can be extremely time-consuming when using exact methods. Execution time is a very relevant factor that often impels the usage of metaheuristics, in detriment of optimality since these allow solving problems in acceptable time scales. The exact methods are associated with integer programming and include the branch-and-bound algorithm, dynamic programming, Lagrangian relaxation, among others. Metaheuristics include, for example, simulated annealing, tabu search, self-adaptive differential evolution and variable neighbourhood search algorithms. Both exact methods and metaheuristics can be combined (Puchinger & Raidl, 2016). Existing works in SCND under uncertainty that focus on the blood domain are recent but scarce. Despite the fact that both supply and demand are uncertain parameters, some works address only uncertainty in demand. This is the case of Ramezanian & Behboodi (2017), Habibi-Kouchaksaraei et al. (2018) and (Haghjoo et al., 2020). Others incorporate operational matters, such as lateral transshipment, which from the point of view of the planning horizon is not appropriate. This is the case of Arani et al. (2021). Still, there are works that, despite modelling the uncertainty in supply and demand, neglect other important issues such as the substitutability between blood types or the selection of the most appropriate capacity for the blood facilities to be established. Examples of these are Samani et al. (2019) and Hamdan & Diabat (2020). Thus, from the literature review presented it is inferred that the topic of blood SCND under uncertainty still lacks research.

3. MODEL FORMULATION

The model presented in this section is based on several works, in particular that of Samani et al. (2019). The major differences between the model of Samani et al. (2019) and the one developed are that the former does not address the substitutability relationships between blood types. Also, the list of variables in Samani et al. (2019) does not include shortage variables as the model guarantees demand satisfaction. This is not the case in the developed model, because it is not possible to guarantee that demand will be fully met if there is not a sufficient supply of either the required blood type or compatible blood types. Decisions affecting the capacity of blood facilities are supported in the work of Cortinhal et al. (2019). This work considers that whenever a facility is established in a candidate location, then a respective capacity level has to be selected. Finally, the environmental component of the objective function of the developed model is supported in the work of Heidari-Fathian & Pasandideh (2018), in the sense that carbon emissions will be directly proportional to variables representing quantities. The model adopts two-stage stochastic programming as an approach to uncertainty. Thus, key strategic decisions such as facility establishment, capacity selection and allocations are made prior to the realisation of uncertainty in the first stage. The remaining decisions are taken in the second stage after the uncertain parameters are known. These decisions include the quantities collected, produced, distributed, among others. The model notation includes the sets, presented in Table 1, the parameters, presented in Table 2, and the variables, presented in Table 3.

Table 1 - Model sets

Notation	Description
I	Set of donor groups indexed by i $(i \in I)$
J	Set of candidate and existing locations for fixed blood collection units indexed by j $(j \in J)$
Q_J	Set of capacity levels available in each potential fixed blood collection unit location indexed by q_j $(q_j \in Q_J)$
K	Set of candidate and existing locations for blood centres indexed by k $(k \in K)$
Q_K	Set of capacity levels available in each potential blood centre location indexed by q_k $(q_k \in Q_K)$
N	Set of mobile blood collection unit locations indexed by n $(n \in N)$
H	Set of demand nodes indexed by h $(h \in H)$
M	Set of blood donation methods indexed by m $(m \in M)$
P	Set of blood products indexed by p $(p \in P)$
B	Set of blood types indexed by b, b' $(b, b' \in B)$
T	Set of time planning periods indexed by t $(t \in T)$
S	Set of scenarios indexed by s, s' $(s, s' \in S)$

Table 2 - Model parameters

Notation	Description
f_{jq_j}	The fixed cost of establishing a fixed blood collection unit located in j with the capacity level q_j
f'_{kq_k}	The fixed cost of establishing a blood centre located in k with the capacity level q_k
e_{jq_j}	The cost of equipping the fixed blood collection unit j with the capacity level q_j
e'_{kq_k}	The cost of equipping blood centre k with capacity level q_k
oc_m	The unit operating cost of blood donation by method m
pc_{pm}	The unit production cost of blood product p collected by the m donation method
ic_{pk}	The unit holding cost of blood product p at blood centre k
ic'_{ph}	The unit holding cost of blood product p at demand node h
$sc_{bb'}$	The unit cost of substituting blood type b with blood type b'
wst_p	The unit wastage cost of blood product p
stg_p	The unit shortage cost of blood product p
tc_{jk}	The unit transport cost of blood packages from the fixed blood collection unit j to blood centre k
tc'_{nk}	The unit transport cost of blood packages from mobile blood collection unit n to blood centre k
tc''_{kh}	The unit transport cost of blood products from blood centre k to demand node h
$ccap_{jq_j}$	The collection capacity of the fixed blood collection unit j with capacity level q_j
$ccap'_n$	The collection capacity of the mobile blood collection unit n
$ccap''_{kq_k}$	The collection capacity of blood centre k with capacity level q_k
$pcap_{pkq_k}$	The production capacity of blood product p in blood centre k with capacity level q_k
$scap_{pkq_k}$	The storage capacity for blood product p in blood centre k with capacity level q_k
$scap'_{ph}$	The storage capacity for blood product p at demand node h
∂_{ij}	The distance between donor group i and fixed blood collection unit j
∂'_{in}	The distance between donor group i and mobile blood collection unit n
∂''_{ik}	The distance between donor group i and blood centre k
∂'''_{jk}	The distance between the fixed blood collection unit j and blood centre k
∂''''_{nk}	The distance between mobile blood collection unit n and blood centre k
∂'''''_{hk}	The distance between demand node h and blood centre k
mdc	The maximum distance between each group of donors and the nearest blood collection unit
mdp	The maximum distance between each fixed or mobile blood collection unit and the nearest blood centre
mdd	The maximum distance between each demand node and the nearest blood centre
φ_m	The percentage of blood collected by method m that is used
δ_{pm}	The production rate of blood product p donated by method m
$\Delta_{bb'}$	ABO/Rh blood compatibility matrix (1 if the demand for type b blood product may be fulfilled by type b' and 0 otherwise)
$\nabla_{bb'}$	ABO group substitution priority matrix
ce_{jk}	Carbon emission rate to transport each unit of blood donated in the fixed blood collection unit j to blood centre k
ce'_{nk}	Carbon emission rate to transport each unit of blood donated in the mobile blood collection unit n to blood centre k
ce''_{kh}	Carbon emission rate to transport each unit of blood product from blood centre k to demand node h
co_2c	Carbon price
s_{bits}	The maximum amount of type b blood that is supplied by donor group i during period t in scenario s
dem_{pbhts}	The demand for blood product p of type b at demand node h during period t in scenario s
π_s	The probability of scenario s
ω	A very large number

Table 3 - Model variables

Notation	Description
Y_{jq_j}	1 if a fixed blood collection unit is established at location j with capacity level q_j; 0 otherwise
Y'_{kq_k}	1 if a blood centre is established at location k with capacity level q_k; 0 otherwise
Z_{ij}	1 if donor group i is assigned to the fixed blood collection unit j; 0 otherwise
Z'_{in}	1 if donor group i is assigned to the mobile blood collection unit n; 0 otherwise
Z''_{ik}	1 if donor group i is assigned to blood centre k; 0 otherwise
Z'''_{jk}	1 if the fixed blood collection unit j is assigned to blood centre k; 0 otherwise
Z''''_{nk}	1 if the mobile blood collection unit n is assigned to blood centre k; 0 otherwise
Z'''''_{hk}	1 if demand node h is assigned to blood centre k; 0 otherwise
V_{bmijts}	The amount of blood type b donated by donor group i by method m in fixed blood collection unit j during period t in scenario s
V'_{bmints}	The amount of blood type b donated by donor group i by method m in mobile blood collection unit n during period t in scenario s
V''_{bmikts}	The amount of blood type b donated by donor group i by method m in blood centre k during period t in scenario s
O_{bmjkts}	The amount of blood type b donated by method m and transported from the fixed blood collection unit j to blood centre k during period t in scenario s
O'_{bmnkts}	The amount of blood type b donated by method m and transported from the mobile blood collection unit n to blood centre k during period t in scenario s
Q_{pbmkts}	The amount of blood product p of type b donated by method m and produced in blood centre k during period t in scenario s
G_{pbkts}	The amount of blood product p of type b produced in blood centre k during period t in scenario s
$U_{pb\prime bkhts}$	The amount of blood product p of type b distributed from blood centre k to demand node h during period t in scenario s to meet the demand for type b'
W_{pbkts}	The amount of blood product p of type b that is wasted in blood centre k during period t in scenario s
W'_{pbhts}	The amount of blood product p of type b that is wasted at demand node h during period t in scenario s
R_{pbhts}	The amount of blood product p of type b in shortage at demand node h during period t in scenario s

The model presents a single objective function that is composed of the cost of establishing blood facilities ($EstC$), the operational cost of collection (OpC), the transportation cost ($TranspoC$), the inventory holding cost ($InvC$), the production cost ($ProdC$), the substitution cost ($SubC$), the shortage cost ($StgC$), the wastage cost ($WstC$) and the environmental penalty due to carbon emissions associated with the network's transport activities ($EnvC$).

$$Minimise\ Z_1 = EstC + OpC + TranspoC + InvC + ProdC + SubC + StgC + WstC + EnvC \quad (1)$$

$$EstC = \sum_j \left(f_{jq_j} + e_{jq_j}\right) \times Y_{jq_j} + \sum_k \left(f'_{kq_k} + e'_{kq_k}\right) \times Y'_{kq_k} \quad (1a)$$

$$OpC = \left(\sum_b \sum_m \sum_i \sum_j \sum_t \sum_s V_{bmijts} + \sum_b \sum_m \sum_i \sum_n \sum_t \sum_s V'_{b"WB"ints} + \sum_b \sum_m \sum_i \sum_k \sum_t \sum_s V''_{bmikts}\right) \times oc_m \times \pi_s \quad (1b)$$

$$TranspoC = \left(\sum_b \sum_m \sum_j \sum_k \sum_t \sum_s tc_{jk} \times O_{bmjkts} + \sum_b \sum_m \sum_n \sum_k \sum_t \sum_s tc'_{nk} \times O'_{bmnkts} + \sum_k \sum_{b\prime} \sum_b \sum_h \sum_p \sum_t \sum_s tc''_{kh} \times U_{pb\prime bkhts}\right) \times \pi_s \quad (1c)$$

$$InvC = \left(\sum_p \sum_b \sum_k \sum_t \sum_s ic_{pk} \times G_{pbkts} + \sum_p \sum_{b\prime} \sum_b \sum_k \sum_h \sum_t \sum_s ic'_{ph} \times U_{pb\prime bkhts}\right) \times \pi_s \quad (1d)$$

$$ProdC = \sum_p \sum_b \sum_m \sum_k \sum_t \sum_s pc_{pm} \times Q_{pbmkts} \times \pi_s \quad (1e)$$

$$SubC = \sum_p \sum_{b\prime} \sum_b \sum_k \sum_h \sum_t \sum_s U_{pb\prime bkhts} \times \nabla_{bb\prime} \times sc_{bb\prime} \times \pi_s \quad (1f)$$

$$StgC = \sum_p \sum_b \sum_h \sum_t \sum_s R_{pbhts} \times stg_p \times \pi_s \quad (1g)$$

$$WstC = \left(\sum_p \sum_b \sum_k \sum_t \sum_s W_{pbkts} + \sum_p \sum_b \sum_h \sum_t \sum_s W'_{pbhts}\right) \times wst_p \times \pi_s \quad (1h)$$

$$EnvC = \left(\sum_b \sum_m \sum_j \sum_k \sum_t \sum_s ce_{jk} \times \partial'''_{jk} \times O_{bmjkts} + \sum_b \sum_m \sum_n \sum_k \sum_t \sum_s ce'_{nk} \times \partial''''_{nk} \times O'_{bmnkts} + \sum_p \sum_{b\prime} \sum_b \sum_k \sum_h \sum_t \sum_s ce''_{kh} \times \partial'''''_{hk} \times U_{pb\prime bkhts}\right) \times co_2c \times \pi_s \quad (1i)$$

Subject to:

$$\sum_{q_j} Y_{jq_j} \leq 1, \forall\, j \quad (2)$$

$$\sum_{q_k} Y'_{kq_k} \leq 1, \forall\, k \quad (3)$$

$$Z_{ij} \leq \sum_{q_j} Y_{jq_j}\ , \forall\, i, j \quad (4)$$

$$Z''_{ik} \leq \sum_{q_k} Y'_{kq_k}\ , \forall\, i, k \quad (5)$$

$$Z'''_{jk} \leq \sum_{q_k} Y'_{kq_k}\ , \forall\, j, k \quad (6)$$

$$\sum_k Z'''_{jk} \leq 1, \forall\, j \quad (7)$$

$$Z''''_{nk} \leq \sum_{q_k} Y'_{kq_k}\ , \forall\, n, k \quad (8)$$

$$\sum_k Z''''_{nk} \leq 1, \forall\, n \quad (9)$$

$$Z'''''_{hk} \leq \sum_{q_k} Y'_{kq_k}\ , \forall\, h, k \quad (10)$$

$$\sum_k Z'''''_{hk} \leq 1, \forall\, h \quad (11)$$

$$\partial_{ij} \times Z_{ij} \leq mdc, \forall\, i, j \quad (12)$$

$$\partial'_{in} \times Z'_{in} \leq mdc, \forall\, i, n \quad (13)$$

$$\partial''_{ik} \times Z''_{ik} \leq mdc, \forall\, i, k \quad (14)$$

$$\partial'''_{jk} \times Z'''_{jk} \leq mdp, \forall\, j, k \quad (15)$$

$$\partial''''_{nk} \times Z''''_{nk} \leq mdp, \forall\, n,k \quad (16)$$

$$\partial'''''_{hk} \times Z'''''_{hk} \leq mdd, \forall\, h,k \quad (17)$$

$$V_{bmijts} \leq \omega \times Z_{ij}, \forall\, b,m,i,j,t,s \quad (18)$$

$$V'_{b"WB"ints} \leq \omega \times Z'_{in}, \forall\, b,m,i,n,t,s \quad (19)$$

$$V''_{bmikts} \leq \omega \times Z''_{ik}, \forall\, b,m,i,k,t,s \quad (20)$$

$$\sum_b \sum_m \sum_i V_{bmijts} \leq \sum_{q_j} ccap_{jq_j} \times Y_{jq_j}, \forall\, j,t,s \quad (21)$$

$$\sum_b \sum_m \sum_i V'_{b"WB"ints} \leq ccap'_n, \forall\, n,t,s \quad (22)$$

$$\sum_b \sum_m \sum_i V''_{bmikts} \leq \sum_{q_k} ccap''_{kq_k} \times Y'_{kq_k}, \forall\, k,t,s \quad (23)$$

$$\sum_b G_{pbkts} \leq \sum_{q_k} pcap_{pkq_k} \times Y'_{kq_k}, \forall\, p,k,t,s \quad (24)$$

$$\sum_b G_{pbkts} \leq \sum_{q_k} scap_{pkq_k} \times Y'_{kq_k}, \forall\, p,k,t,s \quad (25)$$

$$\sum_{b'} \sum_b \sum_k U_{pb'bkhts} \leq scap'_{ph}, \forall\, p,h,t,s \quad (26)$$

$$\sum_m \sum_j V_{bmijts} + \sum_m \sum_n V'_{b"WB"ints} + \sum_m \sum_k V''_{bmikts} \leq s_{bits}, \forall\, b,i,t,s \quad (27)$$

$$O_{bmjkts} \leq \omega \times Z'''_{jk}, \forall\, b,m,j,k,t,s \quad (28)$$

$$O'_{bmnkts} \leq \omega \times Z''''_{nk}, \forall\, b,m,n,k,t,s \quad (29)$$

$$\sum_i V_{bmijts} \sum_k O_{bmjkts}, \forall\, b,m,j,t,s \quad (30)$$

$$\sum_i V'_{b"WB"ints} = \sum_k O'_{bmnkts}, \forall\, b,m,n,t,s \quad (31)$$

$$\varphi_m \times \delta_{pm} \times \left(\sum_j O_{bmjkts} + \sum_n O'_{bmnkts} + \sum_i V''_{bmikts} \right) = Q_{pbmkts}, \forall\, p,b,m,k,t,s \quad (32)$$

$$\sum_m Q_{pbmkts} = G_{pbkts}, \forall\, p,b,k,t,s \quad (33)$$

$$G_{pbkts} = \sum_{b'} \sum_h U_{pb'bkhts} \times \Delta_{bb'} + W_{pbkts}, \forall\, p,b,k,t,s \quad (34)$$

$$\sum_b \sum_k U_{pb'bkhts} \times \Delta_{bb'} = dem_{pb'hts} + W'_{pb'hts} - R_{pb'hts}, \forall\, p,b',h,t,s \quad (35)$$

$$\sum_p \sum_{b'} \sum_b U_{pb'bkhts} \leq \omega \times Z'''''_{hk}, \forall\, h,k,t,s \quad (36)$$

$$Y_j, Y'_k, Z_{ij}, Z'_{in}, Z''_{ik}, Z'''_{jk}, Z''''_{nk}, Z'''''_{hk} \in \{0,1\} \quad (37)$$

$$V_{bmijts}, V'_{bmints}, V''_{bmikts}, O_{bmjkts}, O'_{bmnkts}, Q_{pbmkts}, G_{pbkts}, U_{pb'bkhts}, W_{pbkts}, W'_{pbhts}, R_{pbhts} \geq 0, \forall\, b,b',m,i,j,n,k,p,h,t,s \quad (38)$$

Constraints (2) to (11) concern decisions on the establishment of blood facilities and on the allocation of donors to collcection units and demand nodes to BCs. Constraints (12) to (17) concern the maximum distance between donor groups and blood collection units and between different blood facilities in the SC. Constraints (18) to (20) concern collection sites and state that blood can only be collected from each donor group in the collection facilities to which they are allocated. Constraints (21) to (26) ensure that the capacity of the facilities in the BSC is not exceeded, whether this concerns collection, production or storage capacity. Constraint (27) concerns the donors' capacity to supply blood. It states that the total amount of blood collected from each donor group should not exceed the maximum supply capacity of that donor group. Constraints (28) to (31) concern the shipment of donations to BCs. Specifically, constraint (28) and (29) state that shipments of blood donations from fixed and mobile blood collection units are only possible to the BCs to which they are assigned. Constraints (30) and (31) introduce flow conservation for donations collected in fixed and mobile blood collection units. That is, there is no storage of inventory in these collection units and therefore all donations collected by them must be shipped to BCs. Constraints (32) and (33) relate the donations collected to the resulting blood products after processing. To determine the quantity of each blood product produced, both the utilisation rate and the production rate need to be multiplied by the total amount of donations arriving at the BC. Constraints (34) to (36) concern the quantity of each blood product that is distributed from the BCs to meet demand. Constraint (34) represents the conservation of blood product flow in BCs. The total amount of a blood product produced in a BC in each period must equal the amount of that product that is distributed together with the amount that is wasted, if any. Constraint (35) aims at satisfying demand, although shortage is admitted. Finally, constraints (37) and (38) refer to the domain of variables.

4. CASE STUDY

The Portuguese BSC operates as described in the literature review and its activity is managed and regulated by IPST. IPST estimates that 35 donations per 1,000 inhabitants are needed to meet the country's needs (J. P. A. Sousa & Sousa, 2017). However, the ratio of donations per 1,000 inhabitants has decreased considerably in recent years and has been below the desired value since 2015, thus indicating that the needs for blood products have not always been assured (Escoval et al., 2020; Escoval & Marques, 2020c). The overwhelming majority of donations, around 98%, are WB donations. Concerning apheresis, PLTs are the blood component obtained most often by this method (Escoval et al., 2020). In fact, obtaining the most sought-after blood components through apheresis is a very efficient practice that could have a positive impact on wastage. The most frequent cause of wastage is outdatedness, which may indicate that there is inadequate demand and supply management (Escoval et al., 2020). Table 4 presents the wastage associated with the main blood products in 2019, the most recent data available, this being measured as the difference between units produced and units transfused. The wastage of

PLT pool with pathogen reduction stands out, with more than one-fifth of the units produced being wasted. Still, this is not the most unused blood product. The wastage of PLTs produced from a unit of WB is over 50%, this figure being of great concern (Escoval et al., 2018, 2019; G. de Sousa et al., 2017).

Table 4 - Wastage in the Portuguese BSC according to 2019 data

Blood product	Wastage
RBC concentrate	1.28 %
PLT pool (without pathogen reduction)	6.63 %
PLTs from a unit of WB	57.15 %
PLT pool (with pathogen reduction)	21.05 %

Also, the 2019 data on the distribution of donations at the national level show that there is a marked asymmetry in the donation by region. Table 5 shows the donations collected by region. The IPST line refers to donations collected in BCs and mobile venues. The remaining lines refer to donations collected in hospital blood units. The North region stands out, contributing nearly 20% of the total national donations, a figure similar to the total donations collected in the Centre, Lisboa e Vale do Tejo, Alentejo and Algarve regions. There are also asymmetries between regions in terms of transfusions. The available data on transfusion distribution at the national level refers only to RBC concentrates. In fact, it is observed that the RBC concentrate is the most demanded blood product, being the one that presents the highest number of transfusions and the lowest wastage. Table 5 also shows the units of RBC concentrates transfused by region. It can be seen that RBCs are more demanded in the Lisboa e Vale do Tejo region, followed by the North and Centre regions. Regarding the Lisboa e Vale do Tejo region, it should be noted that transfusions were performed with units coming from other regions of the country, which was also the case in previous years. This situation shows the region's inability to satisfy its needs, as there is a clear imbalance between demand and supply in the Lisboa e Vale do Tejo region (Escoval et al., 2020).

Table 5 - Donations and transfusions of RBC concentrate by region in 2019

IPST/Region	Donations	Transfusions of RBC concentrates
IPST	57.24%	–
Alentejo	3.97%	3.93%
Algarve	3.23%	3.65%
Centre	5.69%	19.38%
Island Portugal	3.04%	3.30%
Lisboa e Vale do Tejo	7.60%	38.60%
North	19.23%	31.14%

Having said that, the generic optimisation model developed is applied to the real case of the Lisboa e Vale do Tejo region in order to understand the performance of the Portuguese BSC in this region.

5. RESULTS

This section describes the computational experiments carried out. These were run using the GAMS modelling system through the IBM ILOG CPLEX 35.2.0 solver in multi-thread mode on a computer with two 6-Core 3.33 GHz Intel® Xeon® X5680 processors with 12 threads and 24.0 GB of RAM. The generic model developed is applied to the Lisboa e Vale do Tejo region using deterministic and stochastic approaches.

Deterministic results

The solution obtained presents a total cost of €135,838,259.71 and the best possible solution of €132,877,450.06. These concern the two-year planning horizon considered. Specifically, four six-month planning periods were studied. The values of the various cost components are presented in Table 6. The components with the greatest share in the value of the objective function are the shortage cost, followed by the production and inventory holding costs. Contrarily, the cost of wastage is the second-least significant. The quite expressive value of shortage was expected, since it is acknowledged that the Lisboa e Vale do Tejo region recurrently experiences a deficit in supply in face of demand.

Table 6 - Cost terms in the deterministic approach

Cost terms	%
Establishment cost	-
Operating cost of collection	2.39
Transport cost	0.28
Inventory holding cost	4.54
Production cost	15.97
Substitutability cost	0.10
Shortage cost	76.66
Wastage cost	0.02
Environmental penalty	0.03

With regard to blood facility establishment and capacity selection decisions, the results show that the model does not establish any new BC. In the case of fixed blood collection units, the set considered did not include any candidate locations. The lowest capacity level was selected for both the BC located in Lisboa and the three existing fixed units, indicating that the current capacity of the facilities is adequate. Production is limited by the donations collected, as expected. There is a significant shortage of RBCs, the most sought-after blood product. The same is not true for PLTs, where there is wastage. However, this is very low, representing only 0.56% of total PLT production. Still regarding this blood product, there are 607 units distributed in a substitution basis. The most substituted blood type is O+ (260 units), followed by A+ (132 units). These are also the most frequent blood types in the Portuguese population. Figure 1 presents the RBC units in short supply. It can be seen that the shortage is also more notable for the most frequent blood types in Portugal.

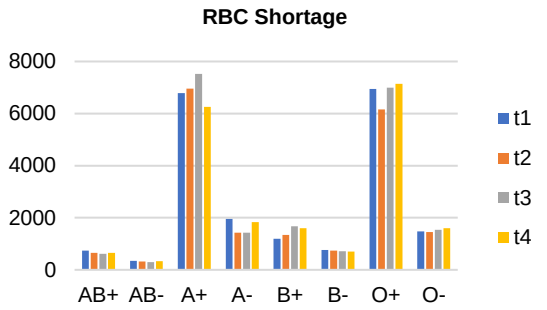

Figure 1 - RBC shortage in the deterministic approach

High shortages of RBCs are not surprising, as it is known that the Northern region of Portugal is where most donations are collected and that the region of Lisboa e Vale do Tejo is where the demand is greatest. The shortage observed could not be reduced by increasing, for example, the capacity of blood facilities, i.e., by selecting capacity level 2. The root of the problem lies in the potential supply from donor groups, which is clearly insufficient to cover needs.

Stochastic results

In the stochastic approach three scenarios are analysed – S3, S4 and S6. S3 combines the estimated 2019 supply with a 10% increase in estimated 2019 demand; S4 combines a 10% reduction from estimated 2019 supply with estimated 2019 demand; and S6 combines a 10% reduction in estimated 2019 supply with a 10% increase from estimated 2019 demand. Scenarios S3 and S4 have probabilities of occurrence of 15%, while S6 has 25%. The solution found has a total cost of €95,649,920.39, with the best possible solution costing €91,761,337.08. Table 7 presents the values taken by the various cost components of the objective function in the stochastic approach under analysis. It is noted that all components take lower absolute values when compared to those previously shown in Table 6. However, the analysis of the relative share of each component in the total cost reveals that shortage takes on greater significance in the stochastic approach than in the deterministic one. Another highlight is wastage, the cost of which is almost zero.

Table 7 - Cost terms in the stochastic approach

Cost terms	%	Comparison with the deterministic approach (Δ%)
Establishment cost	-	-
Operating cost of collection	1.80	↓ 0.59
Transportation cost	0.20	↓ 0.08
Inventory holding cost	3.01	↓ 1.53
Production cost	11.95	↓ 4.02
Substitutability cost	0.06	↓ 0.04
Shortage cost	82.95	↑ 6.29
Wastage cost	0.00	↓ 0.02
Environmental penalty	0.02	↓ 0.01

With regard to establishment decisions and capacity selection, the results are broadly similar to those of the previous deterministic approach. This means that the three existing fixed blood collection units are kept at their current capacity level, as is the BC in Lisboa. The quantities collected in the various collection facilities are close to the maximum supply potential of the donor groups and are more significant in the BC than in the other collection facilities. Following the processing of donations it appears that there is a RBC shortage in all scenarios according to Figure 2. For this blood product there is no wastage. The shortage is more significant in scenario S6 and for the most frequent blood types in Portugal, which would be expected. Regarding PLTs, the stochastic approach shows that there is a shortage, which would not occur in the deterministic approach. However, the shortage of PLTs is much smaller than that of RBCs. Even so, 23 units of PLTs are wasted throughout the planning horizon.

Concluding, the analysis of the three most likely scenarios leads to the conclusion that the observed shortage tends to perpetuate and further increase, resulting in higher costs and lower service level. Nevertheless, as the real case concerns only the Lisboa e Vale do Tejo region, the results should not be extrapolated to the whole country.

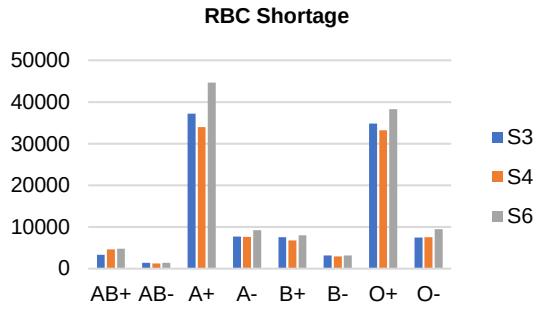

Figure 2 - RBC shortage in the stochastic approach

6. CONCLUSIONS

Past research on the BSC has been dedicated to inventory management. However, recent developments reveal an integrative trend. One of the themes recently addressed, albeit insufficiently, is the SCND. This falls within tactical-strategic planning and is responsible for the location and sizing of SC facilities. It has a profound impact on the efficiency of operations, cost structure and service level. In the case of blood, the network configuration should be designed with an orientation towards meeting demand. In addition, wastage, shortages and operational costs should be considered. The existing literature on BSC management and SCND under uncertainty was reviewed and it was

concluded that many existing network design optimisation models combine strategic and operational decisions. However, at the tactical-strategic level, it does not make sense to plan for the shelf-life of products, for example, which is only a few days for most products. In addition, some of the existing models do not address all echelons of the BSC. Others consider uncertainty only in demand, or only in supply. Also, few models consider the various existing collection methods, the various products derived from WB or the substitutability between blood types. Today, social and environmental considerations are increasingly relevant and should be included in this problem. For all these reasons, there was a need to develop a generic optimisation model that would contribute to the literature to date. Its mathematical formulation was duly described and it was then applied to a real case in the Portuguese BCS – the Lisboa e Vale do Tejo region. It was concluded that the main problem of this region would not be solved with more collection facilities or with more available capacity of the existing facilities, since it lies in the specific supply of the region. The solution currently in force, to cover the existing shortage with surplus production from other regions of the country seems to be the most appropriate.

As for future research, it is suggested to implement the model to larger instances so that the problem can be modelled comprehensively. If this is not possible, metaheuristics are an option to be considered. Although these solution approaches do not allow obtaining an optimal solution, they have a very significant contribution in reducing the time taken to obtain results. Therefore, a combination of exact methods, such as mixed integer linear programming, and metaheuristics is suggested.

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