Planning Blood Collections To Meet Demand And Minimize Waste

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Declaração

Declaro que o presente documento é um trabalho original da minha autoria e que cumpre todos os requisitos do Código de Conduta e Boas Práticas da Universidade de Lisboa.

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I declare that this document is an original work of my own authorship and that it fulfils all the requirements of the Code of Conduct and Good Practices of the Universidade de Lisboa.

Abstract

The Blood Supply Chain (BSC) is a fundamental system since it guarantees the blood supply, an essential good for human life. Nevertheless, such supply chain faces challenges that make its management very complex. The Portuguese BSC is managed by *Instituto Português do Sangue e da Transplantação* (IPST). Among other decisions, IPST is responsible for defining mobile Collection Centres (CCs) routes, location-allocation of facilities, which temporary fixed CCs to open, the schedule for blood withdrawals and the blood quantity to collect. As these decisions impact blood availability, and therefore on health, planning blood collections becomes crucial. In this context, a decision tool to support IPST decision-makers is beneficial.

In this thesis, a mixed integer linear programming model is developed to support IPST on planning collections. The model considers blood perishability and blood group type substitutability. Uncertainty of blood potentials and demand is addressed by implementing a two-stage stochastic programming approach. Within the model objectives, it is aimed at minimizing: distance travelled, wastage, shortage, blood types substitution, transhipment, and the number of temporary fixed CCs to open.

The model is tested considering deterministic and stochastic cases. A sensitivity analysis of a Current Case is conducted by varying blood potentials and demand. Additionally, a Tragic Case is tested to understand the model behaviour when faced with a crisis. Finally, the two-stage stochastic programming approach is tested. A more robust solution is obtained, even with a cost increase of 17% as if uncertainty was known since patient service for different scenarios is ensured.

Keywords: Mobile Collection Centres; Blood Collection; Perishability; Substitutability; Uncertainty; Two-Stage Stochastic Programming Approach.

Resumo

A Cadeia de Abastecimento de Sangue (BSC) é um sistema fundamental pois garante o abastecimento de um bem essencial para a vida humana. No entanto, a cadeia enfrenta desafios que tornam a sua gestão complexa. A BSC portuguesa é gerida pelo Instituto Português do Sangue e da Transplantação (IPST), responsável pela definição das rotas dos Centros de Recolha (CCs) móveis, localização e alocação das instalações, que CCs fixos temporários abrir, calendário das recolhas de sangue e a quantidade a recolher. Dado que estas decisões têm impacto na disponibilidade de sangue e na saúde, o planeamento das recolhas de sangue torna-se crucial. Neste contexto, um instrumento de decisão para apoiar o IPST revela-se benéfico.

Assim, um modelo misto de programação linear inteira é desenvolvido considerando a perecibilidade e substituibilidade do sangue. A incerteza da procura e oferta é tratada através da implementação de uma abordagem estocástica em duas fases. O modelo pretende minimizar a distância percorrida, o desperdício, a escassez, a substituição, as transferências e o número de CCs fixos temporários a abrir.

O modelo é testado considerando casos determinísticos e estocásticos. Uma análise de sensibilidade do caso atual é conduzida através da variação da procura e oferta. Adicionalmente, é testado um caso trágico para compreender o comportamento do modelo quando confrontado com uma crise. Finalmente, a abordagem estocástica é testada. É obtida uma solução mais robusta, mesmo verificando-se um aumento de custos de 17% se a incerteza fosse conhecida, dado que o serviço ao paciente é assegurado para diferentes cenários.

Palavras-chave: Centros de Recolha Móveis; Recolha de Sangue; Perecibilidade; Substituibilidade; Incerteza; Abordagem Estocástica em Duas Fases.

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Table of Contents

List of Figures

List of Tables

List of Acronyms

ASIS Aplicação de um Sistema de Informação a Serviços de Sangue

BC Blood Centre

BSC Blood Supply Chain

CC Collection Centre

DZ Demand Zone

FIFO First-in-First-out

HIV Human immunodeficiency virus

IPS Instituto Português do Sangue

IPST Instituto Português do Sangue e da Transplantação

LIFO Last-in-First-out

MCA Multicomponent Apheresis

MILP Mixed Integer Linear Programmingt

MINLP Mixed Integer Non-Linear Programming

MIP Mixed Integer Programming

RBC Red Blood Cells

VRP Vehicle Routing Problem

WB Whole Blood

Chapter 1: Introduction

This chapter aims to present the master dissertation, introducing the problem to be addressed, this study's goals, and the research methodology. The chapter is organized in three sections: section 1.1 contextualizes the problem under study; section 1.2 outlines the main goals of the dissertation, and finally, the structure of the document is presented in section 1.3.

1.1 Problem Context

The importance of blood to our lives was recognized even before any discovery related to blood. In 1613, the English doctor William Harvey discovered how blood circulates in the body: the heart pumps the blood into the body through the arteries, and the blood returns to the heart through the veins. Since this discovery, blood transfusion experiments have started with the first successful one in 1818 performed by James Blundell. However, during that time, half of the transfused patients had severe reactions. Only in 1901, Karl Landsteiner discovered blood types, so the reactions were due to blood type incompatibility between donor and receiver. The ABO blood group system was then created with four blood types: A, B, AB, and O. These blood types are determined by the presence of substances in the membrane of Red Blood Cells (RBC) and plasma, called agglutinogens and agglutinins respectively. Incompatibility between blood types occurs when a recipient with agglutinin receives blood from a donor with the corresponding agglutinogen. The RBC agglutination process is triggered, the blood circulation is disrupted, and a successful transfusion is prevented. This discovery ended most of the severe reactions that occurred in transfusions. Still, it was not until 1940, when the Rhesus (Rh) blood group system was discovered, that the remaining reactions ended. A person with Rh+ blood has the Rh factor in the RBC membrane. Otherwise, the blood type has a negative sign (-). A person with Rh- blood should only receive a Rh- blood transfusion if no adverse reactions occur (Giangrande, 2000). Once the incompatibility issue was resolved, the need to store the donated blood arose, and the first hospital blood bank was installed in the 1930s. Due to the rapid deterioration of blood affecting the number of transfusions that could be performed, processes and methods were developed to extend the blood shelf-life. Although the shelf-life of blood units has increased nowadays, blood is still a perishable product that disables inventory creation for long periods of time and forces regular replenishment of blood units.

Blood is essential to survival as it performs the function of carrying oxygen and nutrients to the human body's cells. Several proteins, nutrients, hormones, salts, clotting agents, antibodies, and waste products are also present in blood (Lowalekar & Ravichandran, 2014). When extracted from the human body, it becomes a perishable product used for medical treatment. Blood can be separated into four main products, each with a different utility. RBC, platelets, and plasma are used in surgery in case of significant blood loss. Besides, RBC treats anaemic patients and premature infants, and platelets are needed to treat cancer. Plasma has an application in treating liver diseases and burn injuries (Rytile & Spens, 2006). Cryoprecipitate is the fourth blood product. It is originated when the plasma is shortly frozen after collection and later slowly thawed at +4°C ± 2°C. This product is useful for patients with bleeding disorders like haemophilia (Hardwick, 2008).

Considering its importance, patients must receive the necessary blood transfusions without delay. However, maintaining a high service level may lead to an unwanted accumulation of blood inventory. Due to the perishable nature of blood, high inventory levels can translate into high levels of wastage. These are the two main concerns on BSC: blood shortage and blood wastage. Blood shortage refers to when there are not enough blood units to perform transfusions. Shortage is unwanted since it may delay surgeries, untreated patients, and even deaths (World Health Organization, 2017). Blood wastage occurs in consequence of the obsolescence of blood units. As they are not used before the end of their shelf-life, units are forced to be disposed of if not used on time (Özener et al., 2019). As donations are mostly voluntary, blood wastage makes the donor's effort and time in vain. Moreover, donors must respect the deferral time, which is the amount of time that the donor has to wait before making another donation. So, wasting one unit of blood is equivalent to creating a shortage of one unit for the next few months (Lowalekar & Ravichandran, 2014). Therefore, deferral time limits the number of donations that can be made during a planning horizon as well as impacts the schedule of donations made by repeated donors (Özener et al., 2019). A blood unit wasted represents economic loss as all the processes to obtain it had associated costs. Besides, one blood unit wasted in one particular blood bank may result in a shortage at some other blood bank. To mitigate the adverse effects of blood wastage or shortage, the quantity of blood supplied should be chosen to meet demand as closely as possible (Hamdan & Diabat, 2019). Besides perishability, the primary reason why wastage and shortage happen is due to the difficulty of predicting the demand since it depends on patients' needs or, for instance, a tragic event. Donations are necessary to fulfil demand, but as they are voluntary, the blood supply is also unpredictable. Therefore, both supply and demand are uncertain, making it crucial to match supply with demand to avoid wastage and shortage.

Portugal follows the worldwide trend in having an increasingly ageing population that requires more health care (Williamson & Devine, 2013). Hence, the blood demand may increase due to the presence of chronic diseases and comorbidities in society. It is essential to meet the needs of the people by ensuring the right health care service level. Thus, optimizing the processes in the Blood Supply Chain (BSC) is considered of vital importance. A high service level is achieved by meeting demand but simultaneously minimizing blood wastage and shortages along the chain. To do so, blood collection must be planned according to the real supply and demand. Having a proper blood collection planning is fundamental because it is from this activity that the donors' blood becomes available for future use in necessary blood transfusions. Poor planning consequences are product shortages, which prevent transfusions and obsolescence of blood units leading to their waste. For these reasons, collecting enough blood to meet demand without wastage or shortage represents the most considerable trade-off in BSC design. In this context, blood collection planning deserves to be carefully studied. As the collection is the activity that ensures the availability of blood, more effective and efficient solutions must be discovered to enhance the overall performance of the BSC.

1.2 Dissertation Goals

This dissertation aims to develop and use Operations Research techniques to improve the Portuguese BSC regarding blood collection planning to meet the uncertain demand. A two-stage stochastic model is proposed to

minimize blood products wastage and shortage and the total costs associated with blood collection activity while maintaining a required service level. The model provides insights during a planning horizon on routing decisions, location-allocation of facilities that can perform blood withdrawals, temporary fixed CCs to open, scheduling definition, and blood quantities to be collected. Furthermore, and despite being inspired by the Portuguese BSC, the model is general enough to model BSCs with different characteristics from other countries. Secondary research goals include:

- Characterize the Portuguese BSC, highlighting its complex nature and the planning decisions that must be made along the planning horizons.
- Review previous research on BSC planning, focusing on planning blood collections, uncertainty environments and perishable products. These studies are used to support the development of the model.
- Formulate and implement a mathematical optimization model in a context based on the Portuguese BSC data, capable of solving the challenges of blood collections planning and contribute to the existing literature.

1.3 Research Methodology

To achieve the dissertation goals, the research methodology follows the steps outlined in Figure 1.

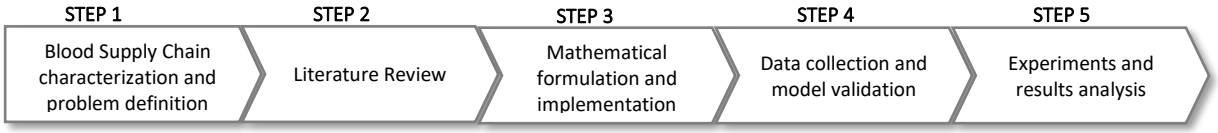

Figure 1 - Proposed Methodology

- **Step 1 – Blood Supply Chain characterization and problem definition**

  This step seeks to introduce the importance of blood and give an overview of BSC properties and functioning. The step also characterizes each one of BSC stages as well as the institution responsible for blood management in Portugal, called IPST. By defining the features and objectives of the BSC and defining the planning process and performance indicators, the challenges of planning blood collections in Portugal and the description of the problem are known.

- **Step 2 – Literature Review**

  This step reviews the literature related to planning blood collections. For this purpose, the types of optimization models dealing with uncertain environments in supply chains are analysed. Due to the perishability of blood, ways to consider this characteristic in models are reviewed. Finally, works on blood collection planning are explored, analysing them regarding the decisions that must be made.

- **Step 3 – Mathematical formulation and implementation**

  After defining the problem and reviewing models in the literature, assumptions are made, and the model is formulated. The development of the decision tool based on mathematical modelling is ensured to reflect the supply chain's needs in Portugal and thus better represent the Portuguese reality. The

proposed model aims to assist planning decisions for blood collections by overcoming BSC challenges such as supply and demand uncertainty, the perishability of blood products and the substitutability between blood group types.

- **Step 4 – Data collection and model validation**

  Relevant data is collected from IPST annual reports and treated regarding the blood collection planning in Portugal. The model is tested to check the validity and ensure accuracy and credibility when applying it to the collected data. The impact of each assumption is also tested. This step is essential for scientific validation.

- **Step 5 – Experiments and results analysis**

  Finally, the obtained results are analysed. The results are then discussed and compared under different scenarios that characterize relevant alternatives regarding mobile CCs routes, location-allocation of facilities, temporary fixed CCs to open, scheduling definition, and blood quantities to be collected. The impact of these scenarios on BSC performance is perceived, and the respective model solution is presented.

1.4 Dissertation Structure

To achieve the goals mentioned in the previous section, the dissertation is organized into seven chapters:

- **Chapter 1 – Introduction**

  This chapter contextualizes and motivates the problem under study, highlights the main objectives to be achieved and outlines the document structure.

- **Chapter 2 – Blood Supply Chain Characterization**

  This chapter introduces important concepts that may help to understand the complex nature of the BSC. It is provided an overview of BSC and each of its stages and an IPST depiction. To understand the problem at hands, trends regarding donations and transfusions in Portugal are presented.

- **Chapter 3 – Literature Review**

  The objective is to review the literature to determine the current best practices dealing with the BSC issues, namely planning blood collection. Therefore, the topics on planning in uncertain environments and planning for perishable products are explored. Then, it is shown how the problem of planning blood collections has been addressed in the literature.

- **Chapter 4 – Model Formulation**

  From the literature review, the insights gathered allied with the Portuguese BSC description are used to develop an optimization model to support decisions for the blood collections planning. The modelling approach and assumptions are detailed. Besides, a solution approach is proposed to enable the model's application to instances where uncertainty must be considered.

- **Chapter 5 – Data Collection and Treatment**

  In chapter 5, the data collection and treatment procedures are detailed. The limitations and the assumptions made to define the instance are described.

- **Chapter 6 – Results**

  Computational experiments are described in this chapter. The model is first applied with a deterministic approach. Then, a stochastic programming approach using scenarios is developed where first-stage and second-stage decisions are considered to address the uncertainty of blood supply and demand parameters. These experiments allow us to make conclusions and findings which are described.

- **Chapter 7 – Final Conclusions and Future Work**

  Hence, the main conclusions are summarized, and future research opportunities are highlighted in the last chapter.

Chapter 2: Blood Supply Chain Characterization

The BSC is a peculiar supply chain since it deals with different challenges. This chapter aims to introduce concepts and properties regarding BSC, which are useful for the remaining chapters. Section 2.1 presents the properties related to BSC, which are the main challenges of its design. Section 2.2 overviews the functioning of BSC regarding its different echelons and stages, and section 2.3 reviews the planning decisions for BSC decision-makers. Section 2.4 characterizes the stages that compose the BSC. Section 2.5 introduces the organization responsible for running the Portuguese BSC, and section 2.6 focuses on the Portuguese BSC structure and shows the evolution of donations and transfusions in Portugal. Finally, section 2.7 presents the problem definition, which introduces what this work tries to solve, and section 2.8 states the conclusions on the chapter.

2.1 Blood Supply Chain Properties

Since blood has a perishable nature, its supply chain presents particular challenges. Perishable products have a short shelf-life which leads to their easy deterioration. The short shelf-life complicates the products supply chain since they must move along it for sale to customers before they perish. After the shelf-life period, products become obsolete since there is a decrease in customer perception of value. These products include fresh foods, dairy products, and pharmaceuticals. However, within perishable products, quality affects the population welfare such as pharmaceuticals, vaccines, and blood products. Thus, blood perishability is a fundamental characteristic that must be considered when designing the BSC.

Blood carries oxygen and nutrients to the human body's cells, which means it is essential to survival. Therefore, there are situations where patients need blood transfusions to recover, such as surgical procedures, continuous or emergency treatments. However, the quantity of blood used in hospitals is impossible to predict since it depends on patients' needs. Thus, blood demand has a stochastic nature since the need for transfusions is uncertain. Besides perishability, this property also adds complexity to BSC design and planning.

Blood is composed of four blood products with different shelf-lives when isolated from the whole blood (WB). Furthermore, the blood products have different therapeutic applications. Table 1 summarizes the shelf-life of blood products and their applications.

Table 1 - Blood and its products characteristics (adapted from Hardwick, 2008)

Blood products	Shelf-life	Therapeutic applications
Whole Blood	30 days	Trauma, Surgery
Red Blood Cells	42 days	Trauma, Surgery, Anaemia, premature infants
Platelets	5 days	Trauma, Surgery, Treatment of cancer
Plasma	36 months	Trauma, Surgery, Liver diseases, Burn injuries
Cryoprecipitate	36 months	Bleeding disorders (e.g., Haemophilia)

For transfusions to be performed, blood must be available. Since there is no substitute for blood, donations are the only way to ensure transfusions. Most of the donations are voluntary and performed by altruist donors. This is a factor that affects and makes the blood supply irregular. That is because the number of donors during a

collection campaign can vary due to the distance they must travel and the level of physical discomfort (Osorio et al., 2018). Thus, as blood demand, the blood supply is uncertain, being another obstacle for BSC planning.

According to the ABO and RhD groups, there are different blood group types in society. However, not every group type is compatible with every patient. When a doctor asks for a blood product, blood units of the same blood group type are selected. Though, when there is a lack of blood units, it is possible to use a different blood group type if this is compatible with the patient. Thus, the substitutability of blood group types is also a singularity of the BSC. To determine the best blood group type to allocate to a patient in need, some rules prioritize blood substitution preferences (Hamdan & Diabat, 2019). Table 2 illustrates the hierarchy of the blood group types that can be donated to each blood group type and received by each group type. The table can be read column by column. For instance, a patient with O- blood group type can only receive from a donor with the same blood group type. Whereas a patient with B+ blood group type should be transfused preferably with its own blood type followed by B- blood group type, then O+ and finally with blood from donors with O- blood type.

Table 2 - ABO and RhD group compatibilities (adapted from Hamdan & Diabat, 2019)

Donor \ Receiver	AB+	AB-	B+	B-	A+	A-	O+	O-
AB+	1st							
AB-	2nd	1st						
B+	3rd		1st					
B-	4th	2nd	2nd	1st				
A+	5th				1st			
A-	6th	3rd			2nd	1st		
O+	7th		3rd		3rd		1st	
O-	8th	4th	4th	2nd	4th	2nd	2nd	1st

As blood is a unique product, and its supply is mostly through voluntary donations, blood wastage becomes unethical. The leading cause of this wastage is obsolescence because the blood units are outdated. There may also be a lack of blood units in the hospital, affecting a patient's life. Therefore, both wastage and shortage may be influenced by blood collection planning. If it is collected too much blood when the demand is not high, then wastage can occur. A shortage occurs if there is a lack of supply, but the demand is high. It is hard to balance this trade-off since both supply and demand are uncertain, so their prediction is inaccurate. Thus, wastage and shortage are the most relevant performance indicators of a BSC.

2.2 Blood Supply Chain Functioning Overview

According to Pirabán et al. (2019), there are five echelons through which the blood flows (see Figure 1). The supply chain's first echelon is the Donors followed by mobile Collection Centres (CCs) and fixed CCs. The third one is the Blood Centre (BC), then Demand Zones (DZs) and finally Patients. As illustrated in Figure 2, the donors go to a mobile or fixed CC or go directly to a BC. Mobile facilities are usually arranged by vehicles prepared to receive blood donations. A shipment of the collected blood goes from all the CCs to the BCs. In BCs, the WB suffers an eligibility test. Depending on the results, the blood is rejected and disposed of or is considered eligible for the next processes. The collected blood suffers separation into its components, being each one necessary for different treatments. They remain stored until a request is made from a DZ, such as hospitals, where patients are waiting for a blood transfusion.

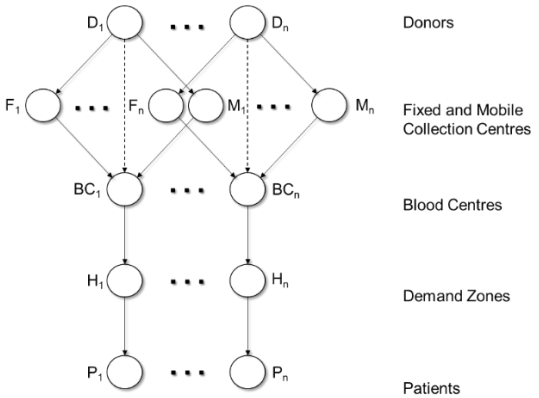

Figure 2 - Echelons of BSC network (adapted from Zahiri et al., 2013)

For an excellent performance of a supply chain, every echelon must be integrated. Precisely, the CCs, the BCs and DZs must be coordinated to perform the different stages related to blood donations. By allowing all the decisions to be coordinated along the entire supply chain, the system can be designed. The design allows all entities to act harmoniously to ensure the objectives are met with minimum costs (Hamdan & Diabat, 2019).

According to Pirabán et al. (2019), six stages summarize the BSC, as seen in Figure 3. The WB is managed in the first three stages, which involve donors, CCs, and BCs. The last three stages, Inventory, Distribution and Transfusion, comprise the BCs once again, hospitals and patients. During this part of the process, the blood is already divided into its products. Although Inventory and Distribution stages are only mentioned at the end of the supply chain, they also occur in hospitals when blood is waiting for a request and between the CCs and BCs, respectively. Between product distinction it is identified a push/pull boundary. As voluntary donors donate the blood, it is difficult to predict the quantity collected. So, as a push approach, WB is collected, and its products are stored before the demand is placed. According to hospitals' daily predictions and requests, the blood is transported from BCs to hospitals representing a pull approach (Christopher, 2011).

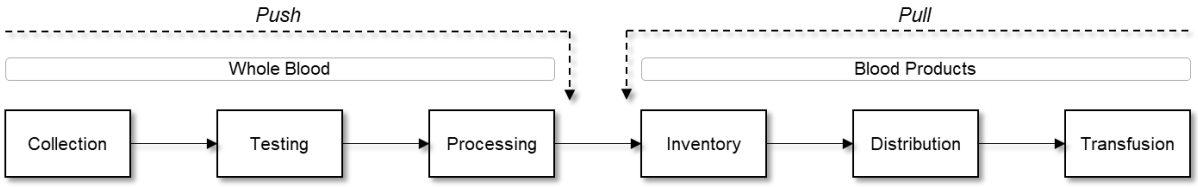

Figure 3 - BSC Stages

2.3 Planning issues for BSC design

To ensure BSC effective functioning, decisions for all stages are made by BSC decision-makers. They must make complex decisions involving multiple resources such as blood collection vehicles, staff, and blood units. Decision-makers seek to minimize costs but ensuring the best service level regarding health care is provided. The decisions are broken down by three hierarchy levels (Osorio et al., 2015): Strategic decisions reflect the long-term strategy of the organization, holding for at least one year; Tactical decisions aim at middle-term planning, valid for one month to one year; Operational decisions are made daily or even in real-time. Figure 4 summarizes the decisions that a decision-maker faces at each decision level. At the highest level, the decisions relate to location and

capacity definition. These decisions affect the tactical level decisions such as planning blood campaigns, staff and collection sites allocation, policy definition, and routing decisions. Finally, scheduling, quantities to order, products to issue, collection methods and transhipment decisions are comprised at the operational level.

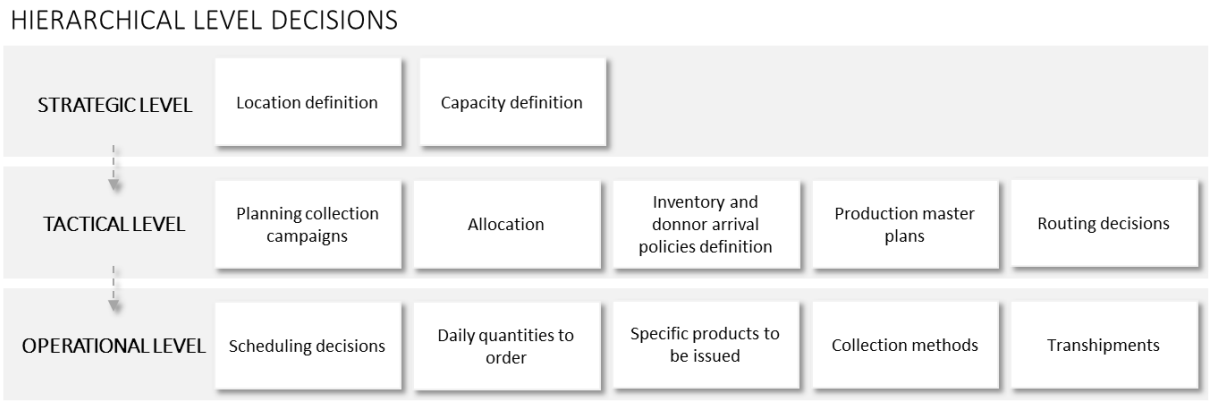

Figure 4 - Hierarchical level decisions for BSC

This dissertation concerns these tactical and operational decisions but focusing on the Collection stage. Moreover, planning blood collections requires matching supply with demand to minimize wastage and shortage. To assist the BSC decision-makers, decision support tools should be developed.

To sum up, BSC design is crucial since it ensures the existence of a product essential to human life. BSC complexity is due to the perishability of blood, the supply and demand uncertain nature, and the chance to replace a blood group type with a compatible one. These factors are some of the BSC challenges. The severity of blood wastage or shortage is influenced by the first three factors mentioned. That is, BSC decision-makers face difficult decisions to ensure a high service level.

2.4 Blood Supply Chain Processes

In this section each one of the six stages that constitute the BSC is explained in detail: Collection (subsection 2.4.1), Testing (subsection 2.4.2), Processing (subsection 2.4.3), Inventory (subsection 2.4.4), Distribution (subsection 2.4.5) and Transfusion (subsection 2.4.6).

2.4.1 Collection

As the first stage of the BSC, the main goal is to attain the right products in the right quantity to meet the demand and prevent a negative impact on human lives. By appealing to the population's goodness and altruism, blood is mostly collected voluntarily, without payment and anonymously. However, donors will rely on the distance they must travel and the level of physical discomfort (Osorio et al., 2018). There are specific conditions for a person to donate blood: a donor must be in good health, have a minimum of 50 Kg, and be between 18 and 65 years old (IPST, 2017b).

Typically, decisions reflecting the long-term strategy are about location and capacity definition. In contrast, in middle-term planning (tactical level), decisions are related to the definition of donor arrival policies, planning collection campaigns and allocation of staff and donors to collection points. The operational level comprises decisions in shorter periods, such as daily decisions, e.g., collection methods for each donor, scheduling, and

collection routes (Osorio et al., 2015). Blood donations can occur at mobile CCs, fixed CCs or BCs. Fixed CCs are decomposed in hospitals and temporary fixed CCs which need to be open. Some hospitals have licences for testing and processing the collected blood for the final user.

Blood can be collected through two methods, each with different costs and impact on the number and type of blood products (Osorio et al., 2018a): WB donations and apheresis. On the one hand, WB donation, which is the most common collection method, consists of attaining 450 cm^3 of blood using a set of collection bags. Single bags store WB while double, triple, and quadruple bags store the separated components. Double bags yield RBC and plasma while triple bags yield RBC, platelets, and plasma. Quadruple bags generate RBC, plasma, and buffy coat (platelets and white blood cells). After the donation, the WB is centrifuged and, depending on velocities and processing times, different components can be obtained using a process known as fractionation. The main components derived from fractionation are RBC, platelets, plasma, and cryoprecipitate. On the other hand, a donation through the apheresis process withdraws a single blood component and returns the remaining blood to the donor. According to Özener et al., (2019), due to recent technological advances, improvements in blood donation allow the extract of more than one blood component with a special apparatus enabling the passage of only required components. It is unnecessary to add a step of separating the donated blood into its components because the final product is ready right after the donation. This method is called Multicomponent Apheresis (MCA).

To compare the efficiency between fractionation and apheresis, one unit of a blood product collected corresponds to one transfusable unit while the fractionation method has a lower proportion. Better than the opportunity to customize MCA donations is the lower deferral time that allows better BSC management. Deferral time is the awaiting time since the last donation until the next one. If a donor makes a WB donation, before making another one, (s)he must wait fifty-six days. However, with the apheresis method, the donor must wait only two days to make the next donation. Therefore, the MCA's main advantage over the WB donation is that more blood products can be collected from a donor during a year. Nevertheless, this new method has disadvantages too. Firstly, it is more expensive, and secondly, the process takes more time from the donor. Finally, donors must meet special conditions in terms of weight (60Kg) and haemoglobin levels (>13g) (Osorio et al., 2018a).

At the end of each collection day, mobile CCs should return to their respective BC with the collected blood. However, in some countries, Portugal is not the case, with the help of shuttles the collected WB is picked up from the mobile CCs and delivered to BCs at regular intervals of time. Shuttles are an improvement because the WB to obtain platelets concentrates and cryoprecipitate must be processed within 8 hours from its donation time. Also, shuttles supply mobile CCs with the necessary inputs for collection activities in the following periods. Therefore, the mobile CCs only need to return to the BC at the end of the planning horizon or the day when it has no more scheduled collection activities at any location (Pirabán et al., 2019).

2.4.2 Testing

Once the collected blood arrives at the BC, it is sent to the laboratory to be tested. This phase is essential to ensure blood safety. First, the ABO and RhD group of each product is determined. It is then necessary to make sure the products are disease-free, so multiple screening tests for each infection type are done (Pirabán et al., 2019). Some of the mandatory tests identify Hepatitis B and Hepatitis C, Human immunodeficiency virus (HIV), Human T-cell lymphotropic virus (HTLV) and Syphilis. Sometimes additional tests are required in certain circumstances. Some donations are also tested for a wider range of blood groups to allow closer matching since they are clinically significant. These tests are made due to the need to reduce the development of alloantibodies in patients who must have long-term RBC transfusion support. Also, blood for neonatal or intrauterine use has a more extensive antibody screen.

In case of success, meaning that the blood units are safe and able to transfusion, the collected blood follows to the next phase - fractionation. After testing and due to infections, a portion of the collected blood products is rejected (Osorio et al., 2017).

2.4.3 Processing

During this phase, the decisions made go through exploring the fractionation alternatives and advantages of collection methods aiming to improve the BSC's performance (Osorio et al., 2015). The approved WB after testing can be either stored for a direct transfusion or separated into its final products which are able to fulfil their very own purpose. There is a vast array of blood products, yet RBC, platelets, plasma, and cryoprecipitate are the most requested ones.

Initially, before the processing, the WB is stored at room temperature for a period of up to 24 hours. To preserve the components' quality, it is necessary to do a faster cooling to room temperature. It uses "cooling" plates filled with a substance at a melting temperature of approximately 20°C the convection streams in the blood bag cause the rapid cooling. This substance is butane-1,4-diol. The plates cool the upper part of the bag while the cold blood at the bottom pushes warm blood upward to meet the plates, thus completing the stream (Van Der Meer & Pietersz, 2007).

It is possible to separate blood components because they differ in density and size. Usually, they are separated by centrifugation, so the constituents sediment at different rates due to centrifugal force. The distribution over the bag occurs as it can be seen in Figure 5. The separation process is dependent on the type of bag used, but it is most commonly used a Top and Bottom bag. Depending on the processing speed/time, different components can be extracted. For instance, if platelet rich in plasma is desired then a lower centrifugation speed for a more extended period would make it easier to select the time to stop. This time to stop is before platelet sedimentation begins. On the other hand, if clear plasma and densely packed RBC are required, a faster centrifuge speed is necessary for an adequate time period.

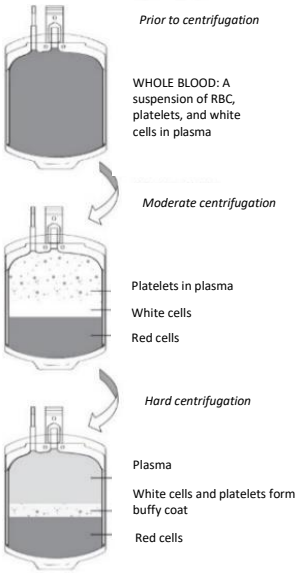

Figure 5 - Centrifugation Process (source: Hardwick, 2008)

After centrifugation, the bag is placed in an automatic machine for separation according to weight obtaining RBC, plasma and buffy coat containing platelets (Hardwick, 2008). Bags are labelled with new information about fractionation and are finally prepared to be stored.

2.4.4 Inventory

Inventory comprises raw material and final products. The former is the blood donated from donors, and the latter is the blood stored and prepared to be transfused. The goal is to maintain an ideal RBC inventory to minimize the outdated units and avoid a shortage which is particularly challenging due to their short perishability. Thus, the indicators for wastage and shortage have a trade-off between them: low inventories cause shortages, but large inventories also lead to blood units' wastage. Hence, the service level may decrease and patients' health can be put in risk (Osorio et al., 2017). The goal can be achieved by optimizing the replenishment policies at the two moments of storage along the supply chain: at BCs where the blood is also processed, and at hospital blood banks (Duan & Liao, 2014).

There are two moments of placing orders for blood: patients needing a transfusion, so doctors place an order to the hospital blood bank, and if a stock replenishment is necessary, the DZ manager makes a request to the BC. In hospitals, the ideal stock level is placed according to their practices and experience. Usually, only RBC are kept in stock while the remaining blood products are ordered by request. There, the inventory is evaluated, and an order is placed from a predetermined ordering point. Overnight the orders are dispatched, and, in the morning, they are delivered. However, there are two types of non-routine delivery: the product demanded is not available, so an emergency order is placed. If the inventory has been depleted, it is necessary to replenish, so an expedited order is made (Katsaliaki, 2008). It is good to have in mind that there are eight different blood group types (ABO and RhD group) with various substitution possibilities. Thus, it adds more complexity to decision-makers when requesting and transfusing blood (Duan & Liao, 2014). Just arrived at the DZ, the requested blood products remain tagged as "unassigned inventory" until an order is placed for a patient. It starts a process known as

crossmatching (compatibility test) after which the crossmatched blood becomes “assigned inventory”. It remains tagged as “assigned inventory” until the operation and for some “safety” time after if not used at that instant. If unused it is moved back to “unassigned inventory”. The time between assigning blood to a patient and returning to “unassigned inventory” is called crossmatch release period.

For a perishable inventory system, the wastage and shortage levels rely on the issuing policy. At BCs and DZs, blood units are sorted and issued in a First-in-First-out (FIFO) order. However, when an unused blood unit returns from the “assigned inventory” it is stored in a Last-in-First-out (LIFO) order. In practice, of all the crossmatched blood only half is actually transfused, and on average an unused unit can be crossmatched around three times before it is used or outdated (Katsaliaki, 2008).

Each blood product has different storage conditions: RBC are separated into a bag with 100mL of an additive solution in the processing stage. The additive solution can support the component's viability and function if stored at +2ºC to +6ºC for up to 42 days from the donation date. Plasma must be frozen resulting in fresh frozen plasma. Within 24 hours from the donation, the freezing must not exceed 1 hour. If stored at temperatures lower than -25ºC, the unit has an expiry date of up to 3 years while at temperatures between -18ºC and -25ºC it only lasts three months. Platelets must be stored at room temperature (+20ºC to +24ºC). Once this is prosperous to bacterial organisms' growth, the expiry date is up to 5 days only. It can be extended to 7 days if bacterial detention tests are performed (Hardwick, 2008). Finally, cryoprecipitate has the same storage characteristics of plasma.

2.4.5 Distribution

Distribution occurs whenever there is blood movement. The first existing distribution is blood products transported from the mobile and fixed CCs to BCs, then from BCs to DZs and finally an internal transference from the hospital blood bank to the point of care. When a vehicle distributes blood from BCs to DZs, it can pick up unused blood products and collect fresh blood from mobile CCs during the return journey to BCs (Pirabán et al., 2019). This stage's purpose is to distribute the right quantity of the right product to the patient at the right time when it is required (Osorio et al., 2015).

Daily, hospitals request blood from their correspondent BC based on historical data, forecasts, and clinical knowledge. Since the request is placed to the BC, blood units’ allocation is made in the morning after, whereas emergency requests arrive throughout the day of the placing order and must be approved by the on-call doctor.

At this stage, long-term decisions relate to the strategy for product delivery, such as choosing vehicle types, capacity, and staff, while the tactical decisions are routing and allocation. Planning at the operational level implies vehicle scheduling, packing, transhipment between different points, and meeting time window constraints (Osorio et al., 2015). Regarding distribution cost, it covers drivers’ salaries, maintenance and fuel expenses, and amortization costs associated with vehicles (Duan & Liao, 2014).

2.4.6 Transfusion

In the transfusion process, a patient should receive his own blood type. However, if not available, a compatible group type must be provided according to the ABO and RhD group. In addition to blood substitute preferences,

there is another criterion to follow: regarding the exact blood group type, the oldest unit but younger than an age α should be transfused first, and secondly, the youngest unit but older than α; regarding a compatible blood group type it follows the same rule. These options are ordered from the most preferred to the least one (Atkinson et al., 2012).

As Duan & Liao (2014) highlight, blood group type compatibilities make inventory management more flexible. That is because it prevents unnecessary outdated units and effectively smooths the match of supply with demand. Nonetheless, Katsaliaki (2008) argues that mismatching blood products is medically considered poor quality of service.

Now that general concepts of BSC design have been defined, the chapter proceeds to describe the Portuguese BSC.

2.5 Instituto Português do Sangue e da Transplantação

In 1958, a structure was created responsible for transfusion medicine, the *Instituto Nacional de Sangue* (INS). The effort was not enough to reach a clear definition of the strategic politic nor effective coordination. In the 80's, some existing inefficiencies start to arise, such as lack of blood and appearance of new transmissible diseases (e.g., HIV). It was time to build a clear and effective national organization with a precise definition of rules to applicate from blood collection to its transfusion for the patient. In 1990, *Instituto Português do Sangue* (IPS) was founded as a public entity with juridical personality and technical, administrative and financial autonomy. IPS integrated services equipped with technical, human, and material resources appropriate to what were or would be their intended functions.

Since 2012, the organization is called *Instituto Português do Sangue e da Transplantação* (IPST). The institution has merged with the transplantation services integrated before by Autoridade para os Serviços de Sangue e da Transplantação. The mission has changed and currently ensures quality and safety regarding not only in transfusion and transplantation medicine activity but also in donation, collection, analysis, processing, preservation, storage, and distribution of human blood, blood components, organs, tissues, and human-derived cells. IPST is split among three decentralized national centres located in Oporto, Coimbra, and Lisbon, covering up different geographic areas, as illustrated in Figure 6. *Centro Regional de Sangue do Porto* (CSTP) covers the northern region; *Centro Regional de Sangue de Coimbra* (CSTC) covers the middle region; regions of Lisbon and Vale do Tejo, Alentejo and Algarve are covered by *Centro Regional do Sangue de Lisboa* (CSTL).

Regarding internal structure, IPST is arranged in three body structures: board of directors, the statutory auditor and the advisory board of blood, histocompatibility, and transplantation. Each regional centre is focused on blood donation promotion, education for blood donation, blood collection, laboratorial area, components storage and distribution, training, hospital articulation and hemovigilance (IPST, 2017b).

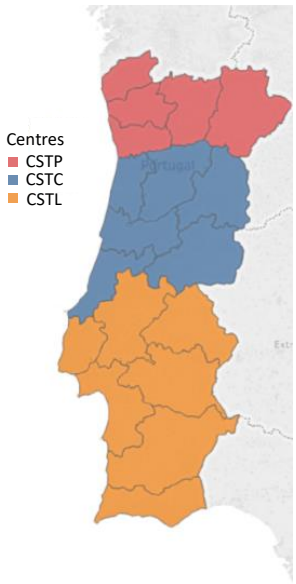

Figure 6 - Distribution of regions per regional blood centre. (source: IPST, 2017b)

In Portugal, 35 voluntary and unpaid donations per 1k inhabitants per year are necessary to ensure national self-sufficiency of blood and its components. Unfortunately, the numbers of donors and donations have decreased, as shown in the next section. Nevertheless, these numbers have the same decline as blood transfusions due to new medical and surgical practices. Even so, IPST has the vision to continue the blood donations promotion to contribute with time and quality for human life. In that sense, IPST promotes good practices and research in transfusion medicine, transplantation, and regenerative medicine. IPST collection activity ensures hospitals' daily replenishment for regular consumption of 4 days and a minimum stock level in each regional blood centre (BC) similar to national consumption of 3 days (IPST, 2017b).

2.6 Portuguese Blood Supply Chain Characterization

In this section, the Portuguese BSC structure is characterized according to what was stated previously (subsection 2.6.1), and it is shown the evolution of donations and transfusions in Portugal (subsection 2.6.2).

2.6.1 Structure

The supply chain network design in Portugal is similar to the one proposed by Pirabán et al. (2019). There are five echelons (Donors, Mobile and Fixed CCs, BCs, DZs, and Patients) and six stages (Collection, Testing, Processing, Inventory, Distribution, and Transfusion) that structure the Portuguese BSC. Donors voluntarily go to mobile or fixed CCs or go directly to BCs where they are able to donate blood. The blood collected by mobile and fixed CCs is transported to the corresponding decentralized national centre of IPST (CSTP, CSTC, or CSTL), according to Figure 6. These centres are the regional BCs of Portugal. In each BC, three stages of the BSC are addressed: Testing, Processing, and Inventory. From these BCs, blood products units are distributed to DZs, where patients are waiting for blood transfusion.

Apart from mobile CCs and BCs, there are twenty-nine predefined fixed CCs, i.e., hospitals. These hospitals work as blood banks since they have established schedules and facilities to conduct WB withdrawals. These hospitals are distributed throughout the country:

- **Northern Region:** Hospital de S. João, IPO Porto, Centro Hospitalar do Porto and Hospitals of Vila Nova de Gaia, Braga, Viana do Castelo, and Vila Nova de Famalicão;
- **Middle Region:** Centro Hospitalar da Universidade de Coimbra and Hospital of Viseu;
- **Southern Region:** IPO Lisboa, Hospital Amadora-Sintra, Centro Hospitalar Barreiro Montijo and Hospitals of Évora, Beja, Portalegre, Litoral Alentejano, Elvas, Faro, Portimão, Torres Novas, Almada, Vila Franca de Xira, and Setúbal;
- **Islands:** Hospitals of Ponta Delgada, Angra Heroísmo, Horta, and Funchal.

These hospitals are responsible for planning their collection schedules. However, campaigns performed by mobile and temporary fixed CCs are planned annually by the corresponding regional BC. The campaigns are scheduled for a particular day in a specific location. Besides BCs, this planning has the collaboration of the donor associations belonging to each region. The donor associations are also responsible for gathering donors and provide the facilities to perform the collection campaigns. The staff selection and the material needed to conduct collection sessions shall be the responsibility of regional BCs. Besides blood donations being voluntary, unpaid and anonymous, tax benefits are granted to both donor and donor association to encourage donations (IPST, 2018).

To ensure integration of information regarding BSC, in Portugal it is used the "*Aplicação de um Sistema de Informação a Serviços de Sangue*" (ASIS) as blood database. With this application, it is possible to manage all activities related to blood promotion and collection (collection campaigns planning, registration of donations and clinical data of donors), processing (separation of blood components, carrying out laboratory tests, qualification of donations), integration of analytical results processed from samples, validation of components and finally their distribution to hospitals in the country (IPST, 2016).

Regarding blood withdrawals, the three blood collection methods are used: WB collection, apheresis, and MCA. In 2019, the apheresis method represented approximately 1.2 per cent of all donations in Portugal, and the MCA method represented 0.3 per cent (IPST, 2019). Despite their advantages, these methods are more time-consuming and are therefore less chosen by donors. When apheresis and MCA methods are used, blood products are ready to be directly transfused to a patient, if after testing, blood units are disease-free. However, when WB is collected from donors, blood is processed to separate WB into its products besides testing.

Once having blood products, it is essential to store them according to their particularities, as mentioned in subsection 2.4.4. Considering their short shelf-life, it is adopted the FIFO methodology to manage inventory. At both BCs and hospitals, there is a minimum inventory level based on the capacity to react to an emergency. At hospitals, it is also specified a stock level according to the hospital's daily activity. When blood units are missing comparatively to the defined levels, hospitals place requests to the respective regional BC. Regarding regional BCs, blood units are transported between centres in case of shortage in one location and over-supply in another.

It must be ensured the distribution for all the hospitals in an uniform way. Therefore, the distribution of blood units starts with the requests made daily by every hospital via ASIS, telephone, email, or fax. Blood bank

technicians register the requests on paper. It is then up to the on-call doctor to allocate the blood units based on some rules that must be followed:

1. At regional BCs, do not distribute over the stock level stated because it is necessary to have enough blood units for emergency requests;
2. At hospitals, requests are made. However, on-call doctors at regional BCs must verify the information in ASIS about the hospital inventory in order to decide if it makes sense to fulfil the need;
3. For hospitals located faraway, regional BCs try to prioritize their needs once it is easier to supply the closer ones;
4. Hospitals with activities such as open Emergency Rooms and maternities have priority in terms of blood supply;
5. Hospitals without blood collections are supplied before the ones with their own blood bank.

The distribution of the blood products units follows the FIFO policy. The expedited units are first verified and validated by the system and then stored according to destination. It is the responsibility of each hospital to collect the allocated blood units. Regional BCs usually accept the return of units up to five days until their expiration date. These units are reallocated, although it is up to hospitals to accept them or not. Suppose a hospital does not have high enough utilization rates. In that case, it is not in its interest to accept older units as the hospital may not have the opportunity to use them and must afford to discard them. Once the patient is ready to receive the blood transfusion, the blood products units are transported from the hospital's storage room to the area where they will be used (Araújo, 2018).

2.6.2 Trends

To understand the BSC's performance in Portugal, it is substantial to know some parameters' values. For that purpose, it was gathered data from (IPST, 2019) focusing on the relevant trends from the past year.

As previously mentioned, Portuguese BSC is powered by voluntary and unpaid donors. Therefore, it is interesting to note the evolution of the numbers of donors and donations. Figure 7 shows that once the number of donations per donor has not changed much, the annual variation of blood donors and donations is the same in the last two years, at least. However, this negative variation is not bad as it comes from applying the approach Patient Blood Management. This approach arose from the need for optimal management when a patient is at risk of transfusion. By supporting new medical and surgical practices that effectively manage the patients' blood, the exceed of blood transfusions is avoided. These practices use haematinics or substances that expand blood volume, minimize blood loss with surgical technique, and optimize anaemia tolerance (Williamson & Devine, 2013).

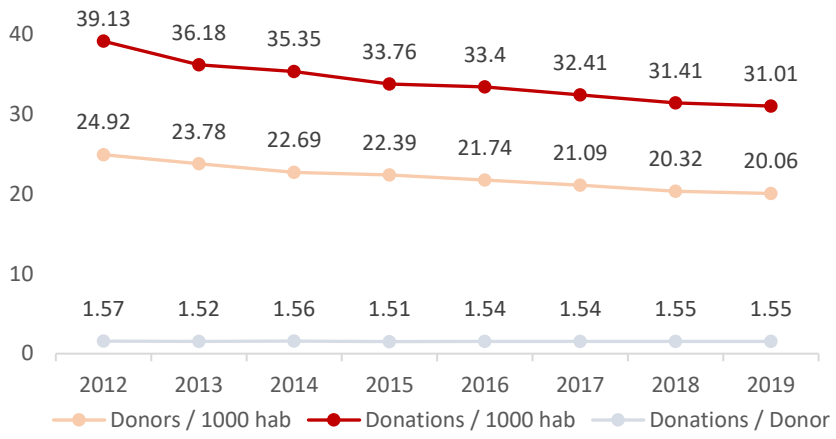

Figure 7 - Evolution of donors and donations values (2012-2019)

Portugal has decentralized BCs, which means that three regional BCs are responsible for the replenishment of blood units in DZs. Thus, it is interesting to understand the collection and transfusion values per region. Table 3 presents values regarding the number and percentages of donations per region and institutions, and the number and percentages of transfusions per region.

In 2019, Portugal had 310 311 donations. However, this value comes only from 54 per cent of the overall registered donors, which is a lower percentage when there are shortages throughout the year. According to blood products transfusion, 74.8 per cent were represented by RBC, then plasma with 12.7 per cent, 12.4 per cent of platelets and finally, less than 0.1 per cent of cryoprecipitate. Once RBC have the highest percentage of transfusion, Table 3 is built only with its corresponding values.

Table 3 - Collections and RBC transfusions trends per region in 2019

IPST / Region	Institutions	Collection	Collection / Region	% of Collection	% of Collection / Region	Transfusion	% of Transfusion
Southern	CSTL	56 160	102 095	18.10	32.9	135 708	46.18
	14 Hospitals	45 935		14.8			
Central	CSTC	48 338	66 004	15.58	21.27	56 968	19.38
	2 Hospitals	17 666		5.69			
Northern	CSTP	73 123	132 789	23.56	42.79	91 511	31.14
	7 Hospitals	59 666		19.23			
Islands	4 Hospitals	9 423	9 959	3.19	3.19	9 705	3.31
Total		**310 311**		100	100	**293 892**	100

One can conclude that IPST has more impact on blood collection than other hospitals. However, the values collected by CSTL do not differ much from the fourteen hospitals of the Southern region. From the blood collected, the highest amount refers to the Northern region, followed by Southern and Central regions, respectively. What can be stated as a big concern is that in the Southern region the percentage of transfusions until the end of 2019 was significantly higher than the percentage of collections performed. Besides, 46 per cent of the transfusions needed are in this region. Therefore, not only demand is stochastic but also demand from the

Southern region cannot be met by the respective blood supply. In this way, there is a need for blood transhipment between this regional BC and others with a higher and positive difference between blood collections and transfusions.

2.7 Blood Collection Planning Problem Definition

After analysing the trends about collection and transfusion in Portugal, it can be concluded that better planning for collections is required since there is a need for a better attempt to meet the stochastic supply and demand throughout the country and hence, to minimize blood shortage and wastage.

The dissertation aims to optimize blood collection planning in Portugal. For proper planning, BSC decision-makers must decide regarding each mobile CC's routes, location-allocation of facilities, temporary fixed CCs to open, scheduling definition, and the blood quantities to be collected. These collection planning decisions must be made considering supply and demand uncertainty, the perishability of the products, the substitutability of blood group types, and the resources constraints of collection facilities. Also, collection decisions must be made considering that multiple facilities and echelons need to be aligned for the same main purpose: the high quality of the patient service level. Therefore, integrability should be assured to avoid the bullwhip effect and minimize the impact of uncertainty on blood collection planning decisions.

2.8 Chapter Conclusions

Along this chapter, concepts and properties regarding BSC are presented. BSC consists of six stages: Collection, Testing, Processing, Inventory, Distributing and Transfusion. Each stage is detailed to better understand the path behind the blood units arriving for patients and at the right level for this work development. The institution responsible for the Portuguese BSC is introduced. It is decentralized in three regional BCs where some of the stages are performed. After presenting the Portuguese BSC structure, some trends related to the chain's former and latter stages are presented regarding Northern, Central and Southern regions. In the North and Centre, the collection percentage is higher than transfusions which means there is blood wastage in these regions. There is an existing problem in the South that there is a higher percentage of transfusions than collections, leading to shortage periods. These issues must be overcome with a better blood collection planning which can be achieved by creating a decision tool to assist decision-makers in planning. This model should give insights on mobile CC routes, location-allocation of facilities, temporary fixed CCs to open, scheduling definition, and the blood quantities to be collected, contributing to the minimization of wastage and shortage while maintaining the service level.

Patient Blood Management initiatives have recently developed a positive climate which may be a step towards a more lasting improvement in shortage problems. However, due to the ageing population worldwide, in the following 5 to 10 years, it may be necessary blood availability to meet the demand. Thus, Portuguese BSC still has ground for improvement.

The next chapter on the state of the art aims to review the existing literature on blood collection planning. This chapter will help understand what approaches can be used to address the problem, which may be useful for developing a methodology to solve the problem.

Chapter 3: Literature Review

To add to the complexity in matching supply with demand, the blood supply is irregular, the demand for blood products is stochastic, and these products are perishable. Thus, there is a sum of challenges when designing a BSC. Shortages lead to an increase in mortality rates. However, outdated units are not accepted by society since blood donors are scarce (Beliën & Forcé, 2012). A recent study on BSC management shows that inventory management is the focus in terms of the number of publications, while collection planning is one of the least studied. Hence, it is important to seek and analyse what was already done to fill the literature gap. This chapter reviews existing literature that helps to understand and solve the blood collection planning problem. Section 3.1 presents the literature review papers on BSC. Section 3.2 presents models that deal with uncertain environments, namely supply and demand. Section 3.3 focus on planning for perishable products, and section 3.4 concerns the planning of blood collections. Finally, section 3.5 presents the chapter's conclusions.

3.1 Earliest Blood Supply Chain Reviews

Only in the 21st century, the first literature review was carried out on BSC. Although Nahmias (1982) has presented a literature review, it was not solely about BSC. Instead of reviewing the literature, Pierskalla (2005) focused on the topic but more as an overview. Thus, Beliën & Forcé (2012) paper is considered the first literature review in BSC. The paper aims to facilitate the tracking of papers published in fields that are of interest, as well as to identify trends and indicate areas for future research. It classifies the literature up to 2010 according to the blood product type, solution methodology, hierarchical level, type of problem and approach, exact versus heuristic, performance measures and, finally, case studies. Several conclusions were drawn from this paper. RBC and platelets were the most studied blood products, and the authors believe the latter is still a fruitful area for further research. That is since platelets are the most sophisticated blood product to deal with due to their characteristics. Most of the studies have used mainly soft computational approaches, such as simulation, statistical analysis, and evaluation/best practices, instead of linear, integer and stochastic programming.

Moreover, authors use simulation approaches since they are more user-friendly to model healthcare supply chains. The focus on the supply chain level has been exceeded by the hospital level or regional BC level. It means that rather than modelling the whole supply chain from all collection locations to DZs, some papers only deal with the hospital or regional BC issues. In addition, there was an increase in publications studying inbound problems being the inventory management category the most studied. Authors suggest that new research will focus on new inventory policies rather than adopting classic inventory models such as fixed order interval policies. Regarding outbound problems, papers describing distribution scheduling problems have been the most popular. Furthermore, papers applying a stochastic programming approach have far outnumbered the papers involving a deterministic setting. This trend will continue since to model BSC the stochastic programming approach is the one that best portrays reality. Concerning exact and heuristic approaches, in the period 2005 – 2010 heuristic methodologies became more popular than exact ones, but the difference was not significant to call it a trend. Hence, there were no predictions about which would receive the most attention in the (near) future. The review also found outdates and shortages as the most used performance measures. There was an

increase in papers optimizing transportation and delivery as well as in donor-related publications and papers on safety and quality. Finally, the authors observed a trend towards papers describing a real-life application of methodologies regarding theoretical papers without any empirical testing and they believe this trend will continue.

Three years later, Osorio et al. (2015) provided a review aiming to present new relevant information for researchers on quantitative modelling for the blood product supply chain. The paper is organized according to four echelons of the BSC (Collection, Production, Inventory, and Delivery) plus an integrated view of the whole chain. For each echelon, there is a description and a representation of decisions and connections to be made at each hierarchical level (Strategical, Tactical and Operational). The authors have contextualized the decisions which have a long-term impact on the Strategical level. This level includes decisions on infrastructure location, capacity, staff and vehicle definition. Decisions for the middle-term planning, such as routing and allocation, inventory policy definition, planning of collection campaigns, production master plans and facilities layout are included in the Tactical level. Finally, decisions that must be made daily (Operational level) comprise scheduling, daily quantities to order, collection methods, how to fulfil demand and transhipments between different points. As a conclusion regarding the collection stage, Osorio et al. (2015) noticed the literature was mainly focused on donor behaviour. The literature was also focused on the location and configuration of blood collection points, but very little on donor allocation to different collection methods. Therefore, the authors propose as further research the study of the cost and efficiency of different collection alternatives, location of mobile CCs, and planning considerations such as periodicity in regular donors. Other problems regarding the other stages also need more attention, such as product allocation to production centres, blood transhipments, best use of substitute products, and the BSC study in an integrated way. Related to the latter, Osorio et al. (2015) found that many of the existent studies focus on a single echelon rather than the whole chain. Therefore, there is a need for further study on integrated models. That is, integrated models can help to identify constraints and bottlenecks between echelons as well as evaluate policies from a whole-system perspective. Finally, due to the complexity of modelling the BSC, the authors realised that it is often necessary to combine methodologies to enhance system performance through a robust decision model.

The most recent paper aiming to provide a review of BSC studies was published by Pirabán et al. (2019) who analysed papers between 2005 and 2019. Unlike Osorio et al. (2015), these authors consider six main processes along the supply chain: Collection, Testing, Component Processing, Storage, Distribution, and Transfusion. The papers are classified by decision-making and forecast environments, issues in the BSC design, operational processes, planning decisions, modelling and solution methods, and data characteristics. Regarding decision-making environments, the authors conclude that most of the papers consider the uncertain environment instead of deterministic. It means the authors realize that in order to try to solve BSC issues supply and demand estimation is fundamental. Pirabán et al. (2019) also noticed, as Osorio et al. (2015), that few papers tackle all the echelons that comprise the supply chain. In this way, it is impossible to avoid the bullwhip effect and minimize the impact of supply and demand uncertainty. Regarding operational processes, some gaps were also found. Only a few papers have considered the apheresis method to obtain blood products as well as the application of

collection policies to prevent excessive inventory levels. Therefore, for future work, the collection methods to be chosen, and the collection fleet's configuration should be studied. From the papers concerning transportation echelon, only one considered the uncertainty in transportation time by shuttles. There should be more focus on this issue as there is a time limit for starting cryoprecipitate and platelet production. The opportunity of having drone delivery of urgent blood products in locations of difficult access is also a field for future research (Scott & Scott, 2018). Storage is the most studied stage, as Beliën & Forcé (2012) had already noticed. Also, only a few papers consider ABO-substitution even this being an inherent feature of the BSC. Finally, as an overall conclusion of the review, authors recommend future works to consider more complex configurations and the study of the interactions between multi-echelon and facilities within an uncertain environment. In addition, the development of efficient solution methods, i.e. hybrid methods such as simulation and optimization or exact algorithms and metaheuristics, will overcome the BSC's complexity.

Figure 8 summarizes the future research opinion from the three review papers on BSC. It can be noticed that from 2012 to 2015 there were improvements since suggestions for future work are not kept. However, from 2015 to 2019 some improvements are made but also some suggestions for future work remain.

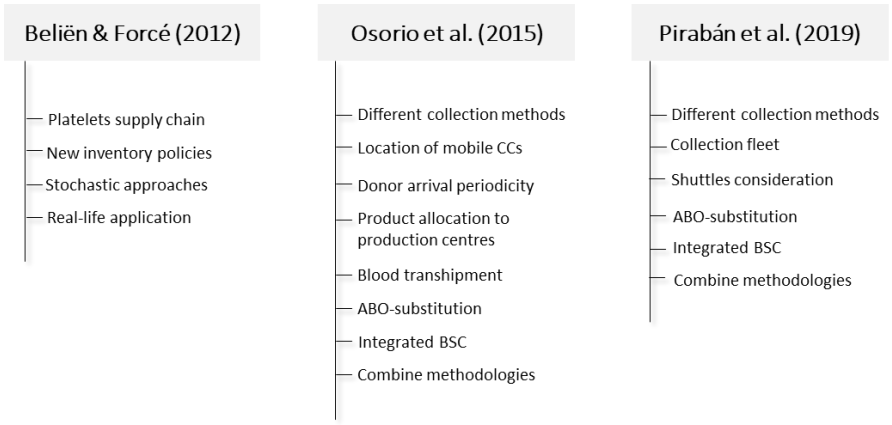

Figure 8 - Future research suggestions from BSC review papers

3.2 Dealing with uncertain environments

Supply chain planning decisions arise in every sector and can be made in the long, middle, or short-term. For instance, most industrial companies plan their decisions based on customer satisfaction. To do so, relevant data should be predicted and described, namely supply and demand. However, many real-world planning problems involve noisy, incomplete or erroneous data (Leung et al., 2007) due to the difficulty of correctly predict supply and demand information. It means that it is essential for proper planning to represent a company's environment as it is. That is, to represent supply and demand, and other parameters involved as deterministic or stochastic. The representation of the environment is a recurring problem that remains to this day in business decisions, mainly in uncertain environments. Nevertheless, it is important because if neglected, the plausible performance of a supply chain in future conditions will be in doubt. Moreover, due to today's rapidly changing global marketplace, it has become essential to include uncertainty in supply chain planning decisions. Thus, this section

aims to understand different ways to model uncertain supply and demand in order to, in the future, try to match them precisely for an application in the BSC design.

Planning models seek to answer questions such as how, how much, when, and where, to match supply with demand. With the answer to these questions, customer satisfaction is met. Once these parameters (supply and demand) are usually uncertain, Govindan et al. (2017) state that there are three main groups of uncertain environments: (1) Decision-making environments with random parameters in which their probability distribution is known; (2) Decision-making environments with random parameters in which decision probability distribution is unknown; (3) Fuzzy decision-making environments. To model these environments, researchers resort to optimization approaches: stochastic programming, including two-stage stochastic programming and probabilistic programming approach, belong to the first group of uncertain environments; robust stochastic programming is used in the second group; and fuzzy programming in the third (Govindan & Cheng, 2018). Therefore, the optimization approaches under uncertainty can be categorized according to two approaches: stochastic programming and fuzzy programming. The following subsections give an overview of each approach and present some cases to understand how they are applied.

3.2.1 Stochastic programming approach

Stochastic programming is a mathematical programming where, unlike deterministic mathematical programming, at least one element present in the data is unknown. Therefore, the uncertainty of the parameters regarded as random variables can be represented by two different methodologies - scenario-based and distribution-based. In the scenario-based approach, a set of discrete scenarios describes the parameters' uncertainty forecasting how this may affect the future. Associated with each scenario, there is a probability level representing the decision-makers' expectation of its occurrence. This approach has the advantage of not having a limitation on the number of considered uncertain parameters. However, it requires anticipating all the possible scenarios that will play out in the future. The latter approach is used only when a continuous range of potential future consequences can be predicted. Assigning a probability distribution function to the range adds complexity to this approach as it limits the number of considered uncertain parameters. However, there is no need to forecast exact scenarios.

Stochastic programming can be distinguished into three approaches: recourse-based programming, robust stochastic programming, and probabilistic programming (Sahinidis, 2004). The first approach is based on the two-stage stochastic programming where the decision variables of an optimization problem under uncertainty are divided into two sets. The first-stage variables have to be decided before the uncertain parameters are realised. Once the random events happen the values of the second-stage variables allow to make other decisions to avoid the problem's constraints becoming infeasible. In other words, the approach requires the decision-maker to assign a cost to recourse activities that are taken to ensure the feasibility of the second-stage problem. This concept of recourse has been applied to linear, integer, and non-linear programming.

The robust stochastic programming, also called robust optimization, proposed by Mulvey et al. (1995) integrates a goal programming formulation with a scenario-based description of input data. The recourse-based model

makes a decision based on the assumption that the decision-maker is risk-neutral (Sahinidis, 2004). The scenario-based approach can tackle the decision-makers' favoured risk aversion (Leung et al., 2007). Thus, it aims to obtain less sensitive solutions to changes in the realization of the input data from a scenario set. An optimal solution of the model is robust with respect to optimality if it remains "close" to optimal for any realization of a scenario – solution robustness. Concerning feasibility, the solution is robust if it remains "almost" feasible for small changes in the input data – model robustness (Mulvey et al., 1995). In other words, this approach seeks to find a robust solution ensuring that all specified scenarios are near-optimum when input data is changed. Regarding the latter approach, unlike the recourse-based approach where the focus is minimizing the expected recourse costs, probabilistic programming focuses on the system's reliability. This reliability is the system's ability to meet feasibility in an uncertain environment, and it is expressed as a minimum requirement on the probability of satisfying constraints (Sahinidis, 2004).

On general supply chain, Bakir & Byrne (1998) develop a stochastic linear programming model to study a realistic planning environment for a multi-product multi-period problem with stochastic demand. The model is based on an equivalent two-stage deterministic problem. However, the demand is modelled as normally distributed with a discrete approximation method. Gupta & Maranas (2000, 2003) propose a two-stage stochastic programming approach to handle demand uncertainty in multi-site supply chain planning problems. The decision variables and constraints of the model are partitioned into production and logistics. The former decisions are made "here-and-now" before the realization of the uncertain demand. In contrast, the latter decisions are delayed in a "wait-and-see" mode as a recourse against the evolving uncertainty demand. In both papers, the demand is modelled as distribution-based. Leung & Wu (2004) develop a robust optimization model to solve the stochastic aggregate production planning problem considering different economic growth scenarios. Leung et al. (2007) extended the model but now to solve a multi-site production planning problem. Thus, for the same goals, production loading plan and the workforce level, several factories' existence was considered. Cholette (2009) investigates a winery's sales channels. Through these multiple channels, wineries often sell wine, each with different packaging and labelling requirements. The authors propose a two-stage stochastic linear programming approach for postponing channel differentiation. Similar to the previous papers, in the first stage, the winery allocates production to intermediate inventory points. Once demand is known, modelled as scenario-based, variables can include the transformation of intermediate inventories to fulfil customer satisfaction. A real-life case of a multinational consumer goods company is studied by Kanyalkar & Adil (2010). The problem plans a multi-site procurement-production-distribution system. The problem is solved by a robust optimization model also based on a two-stage stochastic programming approach. Procurement and production plans are treated as 'here-and-now' decisions while distribution plans can be postponed until the actual realization of the demand. Mirzapour et al. (2011) consider a supply chain with multiple suppliers, manufacturers, and customers, addressing a multi-site, multi-period, multi-product aggregate production planning problem. The authors propose a multi-objective robust optimization model considering uncertainty in both cost parameters and demand fluctuations.

Regarding BSC, Bozorgi-Amiri et al. (2013), Jabbarzadeh et al. (2014) and Salehi, Mahootchi, & Husseini (2017) develop a robust stochastic programming approach to design an emergency BSC facing supply and demand

uncertainties. Ghasemi (2019) also treats disaster situations modelling supply and demand uncertainty with the scenario-based method, but for a location-allocation problem. Zahiri et al. (2014) resort to a robust stochastic programming approach to handle seasonal changes in demand modelled as scenario-based to decide multi-period location-allocation of facilities. Also using a robust optimization approach, Ramezanian & Behboodi (2017) address the BSC design incorporating demand uncertainty. Cheraghi et al. (2017) treat specifically blood platelet production planning. To deal with supply and demand uncertainties, Attari et al. (2018) and Attari & Jami (2018) develop a novel hybrid approach based on stochastic programming, ε-constraint and multi-choice goal programming (first and second paper, respectively), and robust optimization to simultaneously model them. Finally, Zahiri et al. (2018) apply a multi-stage stochastic programming approach to ensure the freshness of transported blood products to hospitals.

3.2.2 Fuzzy programming approach

Fuzzy programming addresses optimization problems under uncertainty, like stochastic programming. However, the approaches differ in the way uncertainty is modelled. Unlike stochastic programming, where the uncertainty is modelled through discrete or continuous probability functions (Sahinidis, 2004), in fuzzy programming, the decision process occurs in a fuzzy environment. It means that the goals and constraints are fuzzy, i.e., goals and constraints can be defined as fuzzy sets in the space of alternatives whose boundaries are not sharply defined. The fuzzy decision may be viewed as an intersection of the given goals and constraints (Bellman & Zadeh, 1970). According to Wan & Dong (2014), there are three main approximations to model uncertain data as fuzzy numbers. The first is a fuzzy programming model with intervals where the decision-maker preference is represented between interval profits defined by a right and left limit (Ishibuchi & Tanaka, 1990). The second is a fuzzy programming model with fuzzy triangular numbers and the third with trapezoidal fuzzy numbers. In these models, a fuzzy number is characterized by three and four values, respectively (Kumar et al., 2011).

Fuzzy programming can be distinguished in two different approaches: flexible programming and possibilistic programming. The former approach assumes that the coefficients' exact values have uncertainty, and some violation of the constraints is acceptable within a specific range. The latter approach involves uncertainty in the constraint coefficients.

On general supply chain, Liang (2006) develop a fuzzy multi-objective linear programming method for transportation problems under the fuzzy available supply and forecast demand. The method also provides a systematic framework allowing the decision-maker to modify the fuzzy data and related parameters until satisfactory solutions are obtained. Thus, it facilitates the fuzzy decision-making process for the decision-maker. Two years later, Liang (2008) extended the study to integrate multi-product and multi-time period production/distribution planning decisions. This paper aims to minimize distribution costs and time dispended but now concerning inventory levels, available labour levels, machine capacity at each source, forecast demand, warehouse capacity at each destination, total budget, and the time value of money for each cost categories. Aliev et al. (2007) also seek to model a fuzzy integrated multi-product and multi-period production/distribution but for an aggregated planning in a supply chain with uncertain customer demand and production capacities. Peidro et al. (2007) solve a planning problem under supply, process, and demand uncertainty in a real automobile supply

chain. The data are not well known and therefore modelled by fuzzy triangular numbers in possibility theory. The fuzzy model allows the decision-maker to plan alternative decisions regarding different grades of possibility. A crude oil supply chain network design problem is addressed by Jabbarzadeh et al. (2016) who propose a multi-period fuzzy mathematical programming model. The uncertain parameters, including demand, are represented as fuzzy sets. To optimize the use of water and land resources for irrigation, Ren et al. (2017) developed a multi-objective possibilistic programming method considering administrative, economic and ecological benefits as planning objectives. Since it is applied a possibilistic programming method, optimal irrigation plans were obtained under different possibility levels of fuzzy sets.

Regarding BSC, Zahiri et al. (2013) apply a robust fuzzy programming approach to deal with uncertainty when making decisions over a multi-period regarding location-allocation of facilities. Samani & Hosseini-Motlagh (2018) and Zahiri & Pishvaee (2017) use the same approach to ensure a consistent BSC network reliability and robustness at a minimum cost. Rabbani et al. (2017) find the best mobile CCs location routing regarding the system for platelet production, considering the number of donors as a fuzzy parameter.

3.3 Planning for Perishable Products

Since this work purpose is planning blood collections, it is essential to understand how to deal with product perishability. Therefore, this section aims to realize how planning for perishable products has been carried out in the industry in general. The aim is to know different approaches and apply them in the model being developed in this work. This section presents different notions of perishability and several models in which it is considered.

A perishable product is characterized by at the end of its shelf-life, the product no longer has any value for the consumer, being spoiled. The shelf-life is defined as the period during which the commodity remains suitable for consumption. The perishability issue came up by Nahmias (1982) with inventory modelling in a blood bank. Meanwhile, considering perishability in other products seemed interesting, for instance, in newspapers, fashion clothes, chemicals, drugs and food (Wei et al.,2019). It became evident that it would have to consider the product's exact characteristics to ensure more strategic and optimal solutions for a system to be correctly modelled. Thus, over the years there were reviews concerning perishability. Nahmias (1982) distinguish two types of perishability: fixed lifetime and random lifetime. Products whose shelf-life is previously known and independent of other parameters have the former type, for instance, milk, yoghurt, and blood in inventory. The latter type of perishability refers to products with an unknown shelf-life which is assumed to be a random variable with a probability distribution, for instance, fruits, vegetables, and flowers. The author studied the ordering policies and inventory management for both types of perishable products, considering deterministic and stochastic demand. More recently, Amorim et al. (2012) focus on developing production and distribution models considering perishable products. The authors identified four approaches: (1) consider a make-to-order strategy avoiding spoiled products; (2) constrain the number of periods a product can be in stock; (3) use different holding costs according to the remaining shelf-life of the product; and (4) attribute a value to the different degrees of freshness when the product is delivered. By applying a multi-objective mixed integer programming (MIP) approach, Amorim et al. (2012) study the advantages of integrating the analysis of production and distribution

planning in economic and freshness terms. One year later, Amorim et al. (2013) extended the study to give a new framework for perishability models composed of three classifying dimensions: Physical Product Deterioration, Authority Limits, and Customer Value. This new framework gives an accurate picture of the perishability phenomenon affecting a product. Consequently, the framework points towards the essential mathematical modelling issues to be considered.

Increasingly, researchers start to give importance of considering perishability in the production process. Entrup et al. (2005) develop a MIP model that integrates shelf-life issues into production planning and scheduling in yoghurt production by adding a term to the objective function related to the product value. This product value is based on shelf-life. Naso et al. (2007) try to solve production and distribution scheduling of a network of plants supplying perishable materials. Since the product is rapidly perishable, it is produced on demand and delivered within the time window specified by customers. However, one of the main challenges is to avoid delays that exceed the shelf-life of the product. The major disadvantage of these models is not considering an uncertain environment. Leung & Ng (2007) solve the production planning for perishable products with postponement through a pre-emptive goal programming model. This approach is usually used to manage a set of conflicting objectives by minimizing deviations between target values and realized results. To deal with perishability, the authors divide the production process into two phases postponing the final assembly in the later period of the planning horizon to meet fluctuations in demand. Leung et al. (2007) solve the same problem but applying a robust stochastic programming approach. An optimal production plan is obtained assuming a future economic scenario with an associated probability. Chen et al. (2009) consider production scheduling and vehicle routing with time windows for perishable food products through a nonlinear mathematical model. The model aims to find the optimal production quantities, the time to start producing and the appropriate vehicle routes, under stochastic demand. If a vehicle arrives late, a penalty cost is incurred. Also, to handle perishable food products, Amorim et al. (2013) develop a two-stage stochastic production planning model. The main goal is to explore the trade-off between the risk of spoilage and the risk of revenue loss with stochastic parameters related to the demand, consumer behaviour, and the spoilage effect. Therefore, the authors develop a risk-averse production planning model that incorporates financial risk measures. Susarla & Karimi (2012) study the integrated supply chain planning for multinational pharmaceutical enterprises. As some pharmaceutical products are perishable, the paper considers the shelf-life as the duration after production for which the material remains suitable for use or consumption. To ensure a product is not used after its expiration date, material's age is tracked from its production until the end of its shelf-life and beyond. Van Elzakker et al. (2014) address tactical planning optimization for the Fast Moving Consumer Goods industry. To do so, shelf-life restrictions are considered by either tracking the age of end products, like the previous paper mentioned or forcing them to leave inventory before the end of their shelf-lives. Wei et al. (2019) recently decided to incorporate perishability issues in a multi-level lot-sizing and scheduling problem. It is the first paper considering the perishability of raw materials, intermediates, and end products simultaneously. The authors believe that by tracking their shelf lives at each production level, the overall production management can be improved.

Regarding BSC, Nagurney, Masoumi, & Yu (2012) present a model to manage the supply chain network operations that capture blood's perishability through arc multipliers. Gunpinar (2013) minimizes shortage and wastage levels at a hospital within a planning horizon considering that the age of platelets and RBC units received from the BC is known and varies over time. Dillon, Oliveira, & Abbasi (2017) proposes a two-stage stochastic programming model for inventory management, considering blood perishability and blood substitutability. Blood age is followed by the time periods in which blood pack units are collected comparing to the time period in hand. Araújo, Santos, Marques, & Barbosa-Povoa (2020) present a model for the blood supply chain's tactical and operational planning but considering the blood collected as an input. Multi-products, multi-periods, multi-echelons, and perishability in an extensive planning horizon are considered for a real representation of BSC.

Having addressed how to deal with uncertain environments and the perishability of products, it makes sense to move forward with planning blood collection when designing its supply chain.

3.4 Blood Collection Planning

Both supply and demand are uncertain in the BSC network. Planning blood collections is the operation where matching supply with demand is most important. It means that the correct modulation of supply and demand uncertainty is necessary to ensure blood products' availability when needed. Since blood collection is the first activity in the supply chain, and only from it is the product available for use, its performance must be excellent. Thus, if the planning of blood collections is not well done, flaws will spread along the chain. Planning collections encompasses several decisions (Osorio et al., 2015): donor arrival policies; staff allocation; routing decisions; facilities location-allocation; scheduling definition; and finally, blood quantities to be collected. Besides, the BSC effectiveness can be measured by performance indicators such as wastage and shortage levels and collection cost. Proper planning is also characterized by a realistic matching of supply with demand. The remaining of this chapter discusses studies distinguished by the decisions that must be made to plan blood collection: section 3.4.1 presents papers studying donor arrival policies and how staff should be allocated to assist in the donation process; section 3.4.2 regards mobile CCs routing decisions; section 3.4.3 shows studies that decide on facilities location-allocation which means deciding on the location of each mobile or temporary fixed CC during a planning horizon and the allocation of donors to these; section 3.4.4 addresses other decisions that can be made to improve the blood collection planning; section 3.4.5 presents papers focusing on improving performance indicators and finally, section 3.4.6 shows why the present work is relevant for the BSC literature.

3.4.1 Donor arrival and staff allocation

The blood collection process starts when a donor arrives at a blood collection facility. The donor is registered and visited by a staff member to aid in the donation process if the donor is eligible. A collection facility may or may not have a reservation system. Thus, donors can be divided into booked donors and walk-in donors. The former set aside a specific time slot to avoid long waiting times and queues. At the same time, the latter show up without a reservation. There is a further division: regular or occasional donors. The former regularly donate while the latter occasionally donate, both after the deferral time established by law. Therefore, it is important to consider

the donor arrival when planning blood collection as well as the staff allocation for mobile CCs to ensure donor support (Güre et al. 2018).

Pratt & Grindon (1982) study workflow and queueing problems using a computer simulation model and compare donor scheduling strategies with random arrival. Brennan, Golden, & Rappoport (1992) develop a simulation to study the customer service and productivity issues of Red Cross mobile CCs. Since excessive waiting lines affect donors' willingness to make subsequent blood donations, the authors tested several strategies. These strategies are to alleviate the waiting lines modifying set-up, staff allocation, and work rules. Michaels et al. (1993) develop a simulation also for Red Cross mobile CCs to evaluate strategies for scheduling donors' arrival comparing them in terms of mean transit time to find out the most effective one. Improving the scheduling system leads to efficient use of staff resources and donors' satisfaction. Bretthauer & Côté (1998) use a combination of integer linear programming and basic queueing theory to determine the size of the nursing and support staff necessary to avoid excessive donor waiting times. Ferguson & Bibby (2002) predict the number of future blood donations using a prospective design. Intentions were predictive for occasional donors, and past behaviour was predictive for regular donors. By using annual donor retention rates and mean numbers of donations per donor and year, Borkent-Raven, Janssen, & Van Der Poel (2010) estimate the blood supply from donations. Testik et al. (2012) adopt clustering, classification, and regression tree methods in succession to identify donors' arrival patterns. By applying a queuing network model, the workforce utilization in the blood donation process is balanced. Boonyanusith & Jittamai (2012) use an online questionnaire to investigate donors' behaviour patterns. The authors also evaluate the factors that influence donation decisions such as altruistic values, knowledge in blood donation, perceived risks, attitudes towards blood donation, and intention to donate blood. Alfonso et al. (2012; 2013) use data from the French National Blood Service and propose a simulation-based approach to describe the distribution during the day of walk-in donors. Then, decisions on the best configurations of blood collection systems regarding human resources capacity and appointment strategies are made. Alfonso, Augusto, & Xie (2013;2015) address the planning of blood collections regarding the expected number of donations at each mobile CC and the human resource requirements including secretaries, physicians, nurses, and drivers. Predictions are based on demographics (number of potential donors), donor generosity (number of donations a donor is willing to give each year), and donor availability (the probability that a donor is available during mobile collection campaign).

Regarding human resource capacity, it is assumed to be independent since mobile CCs need considerable setup time for transportation and equipment installation. Blake & Shimla (2014) present a method to calculate staffing requirements while minimizing costs and ensuring donor wait time metrics are met. van Dongen et al. (2014) analyse the factors that influence new donors to continue donating. Ritika (2014) analyses different classification algorithms to determine the classification technique with the best accuracy rate and the least error for the blood donors' prediction. Alfonso, Xie, & Augusto (2015) propose a simulation-optimization approach for capacity planning and appointment scheduling considering random arrivals of walk-in donors, and random no-shows of scheduled donors. To maximize platelet production, Mobasher, Ekici, & Özener (2015) propose a mixed integer linear programming (MILP) model to coordinate pick up and appointment schedules at the mobile CCs taking

into account the processing time requirements for platelet production. More recently, Baş et al. (2017) propose an appointment scheduling framework consisting of pre-allocating time slots to blood group types which are then filled when the donor calls to make the reservation. The approach aims to balance the production of the different blood group types units over a time horizon to provide constant feeding of blood units to the blood donation system.

3.4.2 Routing decisions

During a collection campaign, the mobile CCs have to visit specific locations to collect blood from the donors. Thus, each vehicle follows its assigned route, which is defined for a planning horizon. In some countries, the BSC also includes shuttles to pick up the collected blood from mobile CCs and deliver to BCs. These vehicles ensure platelets' production concentrates and cryoprecipitate on time since these blood products must be processed within 8 hours from its donation time. Therefore, it is also necessary to define routes for shuttles.

Doerner & Hartl (2008) and Doerner et al. (2008) focus on Austrian Red Cross blood collection operations regarding a Vehicle Routing Problem (VRP) for shuttles. The problem is defined with multiple interdependent time windows since the authors consider the shelf-life of the donors' collected blood. Gunpinar (2013) solves the VRP for mobile CCs using CPLEX solver, branch-and-bound and column generation algorithms. The solutions times are compared as well as the minimization of daily distance travelled. For the Turkish Red Crescent blood collection system, Şahinyazan et al. (2015) develop two MIP models. One model aims to determine the best tours of mobile CCs and shuttles to minimize transportation costs. At the same time, the other decides on the duration of each visit. To solve both models more efficiently, i.e. with a decrease in computational time while still providing near-optimal solutions, a heuristic algorithm was designed. To determine a set of locations among a group of potential sites for blood collection so as to avoid shortfalls, Gunpinar & Centeno (2016) develop an integer programming approach to solve the VRP. The model identifies the number of vehicles necessary to deploy each day and minimize travel distance considering variable visits duration, uncertainty in blood potentials and multiple vehicle types. The solutions for large instances are solved with a branch-and-price algorithm. Rabbani et al. (2017) cover the blood collection planning problem for platelet production. The model finds the best tours for shuttles and mobile CCs while minimizing the logistics costs. Solutions are obtained using a Simulated Annealing (SA) metaheuristic approach. Ramírez, Rueda, & Labadie (2018) adapt the VRP with profits to minimize the total routing, wastage, and shortage costs. The problem is represented using a scenario-based approach where the blood supply follows a Poisson distribution function. The fast-forward selection algorithm is implemented to reduce the set of scenarios. Finally, Hoang (2018) develops three models for mobile CCs in Ho Chi Minh City. The first and second models use MILP to design a single route for mobile CCs to collect the maximum desired blood with minimum transportation cost. The third model is modelled as a VRP for mobile CCs and shuttle. This last model has better performance regarding the total transportation cost and time savings than the other two models.

3.4.3 Location-allocation decisions

Typical supply chain design decisions involve determining the optimal location to satisfy the market demand at the lowest cost. In contrast, BSC is a dynamic network. Although possible facilities locations are already defined by the institution responsible for blood collection system decisions, it is necessary to adjust during a planning horizon. These adjustments are to address potential supply and demand fluctuations and variations in key input parameters. Therefore, the planning horizon in the BSC is divided into several time periods, and location-allocation decisions are made periodically.

Şahin et al. (2007) study the redistribution of mobile CCs in the regionalization of Turkish Red Crescent blood services for a single period. Ghandforoush & Sen (2010) propose a decision support system for planning platelets production aiming to minimize costs as well as improve the blood collection schedule. To make strategic and tactical planning decisions over a multi-period, Zahiri et al. (2013), Zahiri, Mousazadeh, & Bozorgi-Amiri (2014), Ramezanian & Behboodi (2017) and Zahiri & Pishvaee (2017) use mathematical programming models. These models consider a multi-period location-allocation problem where decisions such as the location of mobile CCs among a given set of potential sites and the assignment of donors to the facilities are made. The difference between Ramezanian & Behboodi (2017) model to others is that its goal is to increase utility and motivate blood donors to donate blood. Thus, parameters include social aspects such as donors' distance to blood collection facilities, experience factor of donors in these facilities, and their advertising budget. Cheraghi et al. (2017) treat the integrated processes of blood platelet production planning. Sha & Huang (2012), Jabbarzadeh et al. (2014), Salehi et al. (2017), Samani & Hosseini-Motlagh (2018) and Ghasemi (2019) design an emergency BSC for disruption scenarios such as disaster situations to make multi-period location-allocation decisions. Sha & Huang (2012) propose a ‘p-median’ model assuming that the number of blood collection facilities is known before the disaster. Such anticipation is not valid in real cases and thus, restricts the usefulness of the model. To test the case study regarding Beijing, the authors use a heuristic algorithm based on Lagrangian relaxation. Jabbarzadeh et al. (2014) and Salehi et al. (2017) adopt a two-stage stochastic programming approach where permanent facilities' location is determined in the first stage. Mobile CCs location and the allocation of blood donors are decided after the disaster scenario. Attari et al. (2018) and Attari & Jami (2018) design the blood collection and distribution network through a bi-objective MILP formulation. Heidari-Fathian & Pasandideh (2018) recommend designing an integrated green network through a model that minimizes the supply chain's total environmental effects due to transportation activities. To deal with the model's complexity, the authors apply a Lagrangian relaxation heuristic to achieve near-optimal solutions for more significant instances.

3.4.4 Other planning decisions

Besides deciding on donor arrival policies, staff allocation, mobile CC routes and facilities location-allocation, other decisions complement the blood collection planning. Osorio, Brailsford, & Smith (2018), Osorio et al. (2018) and Özener et al. (2019) consider in their models the collection method used to obtain blood and its products, i.e., WB donation or apheresis method. Özener et al. (2019) added the MCA method since MCA increases donor utilization and hence ensures better BSC management. That is due to changes in blood supply and demand,

deferral times and perishability of blood products. Lowalekar & Ravichandran (2010), Zahiri & Pishvaee (2017), Osorio, Brailsford, & Smith (2018), Osorio et al. (2018), Ghasemi (2019) and Hamdan & Diabat (2019) present their models considering the ABO compatibility and substitution permissibility. The decision on the fleet size of a mobile CC during a planning horizon is addressed by Şahin et al. (2007) and Samani & Hosseini-Motlagh (2018). Şahin et al. (2007) consider a homogenous distribution of mobile CCs to reduce their inefficiency and balance fleet sizes concerning regional populations. In contrast, Samani & Hosseini-Motlagh (2018) design a BSC determining the optimal number of mobile CCs under disruption scenarios. Despite never having been mentioned in papers, some BSCs address the decision to open temporary fixed CCs with the same goal of mobile CCs: to reach all the population quickly. The Portuguese BSC is one of these BSCs, i.e., IPST must open temporary fixed CCs and define its schedule (Dador, 2020). Finally, regarding blood quantities to be collected, this decision is addressed in all papers related to blood collection.

3.4.5 Performance indicators

Performance indicators are essential for planning and controlling supply chain processes, making it possible to set targets since the results are fundamental for decision-making. Performance indicators serve to work efficiently in achieving the defined objectives. Therefore, it is essential for efficient blood collection planning to ensure minimum wastage and shortage level at a minimum collection cost.

Cumming et al. (1976) and Pegels et al. (1977) propose a model to eliminate periods of shortage or oversupply of predictable blood potentials once blood collection operations have been planned. In both papers, the authors conclude that when rescheduling collections, the variability of inventory decreases dramatically. This rescheduling significantly reduces shortages with little increase in cost or age of transfused blood. Therefore, there is an improvement in quality and quantity service. Lowalekar & Ravichandran (2010) realise through a simulation model that by cutting off the supply level, a blood bank could reduce a considerable number of wastages without significantly increasing the shortages. Cutting off the supply level is not accepting more blood donations at a campaign once the cut-off level is reached. The level depends upon blood availability during a given month. The extra units can be given to other blood banks that face blood shortages. Sha & Huang (2012) propose an emergency blood supply scheduling model considering a penalty cost in the objective function to avoid shortages. Nagurney, Masoumi, & Yu (2012) consider costs associated with shortages as well as the discarding cost of the outdated product at the demand points due to the possible excess supply delivered. Gunpinar (2013) minimizes shortage and wastage levels of blood products at a hospital. If demand is not satisfied due to the unavailability of blood units, a shortage cost is incurred. If a blood unit expires, a wastage cost is incurred associated with discarding blood units. Ramezanian & Behboodi (2017) attempt to increase blood donors' utility in order to reduce shortages. Zahiri & Pishvaee (2017) present a model that minimizes shortages and total system costs without minimizing the outdated units. This limitation is due to considering the perishability of blood products only by limiting the transportation time to be less than the product's shelf-life. Osorio et al. (2017) aim to minimize wastage and shortage level through an integer linear programming model. The model calculates the optimal required number of donors each day by blood group type and collection method. The model incorporates uncertainty in supply and demand, based on probability distributions fitted

from historical data routinely collected in all BCs. Ramírez, Rueda, & Labadie (2018) minimize the total wastage and shortage costs. Regarding collection costs, several papers try to minimize them such as Lowalekar & Ravichandran (2010), Alfonso et al. (2012; 2013), Osorio et al. (2017), Samani & Hosseini-Motlagh (2018), Osorio et al. (2018) and Özener et al. (2019). Alfonso et al. (2012; 2013) also perform an analysis of cost-effectiveness defined as service level divided by total cost.

3.4.6 Summary of the literature on Blood Collection Planning Problems

As the current project consists of planning blood collection to meet demand and minimize waste, this subsection compares papers mentioned in the chapter addressing most of the BSC features to consider in blood collection planning. Table 4 presents the main characteristics of the respective models of the selected papers: the decisions the paper makes (Donor Arrival policies, Staff Allocation, Routing, Location-Allocation, Scheduling, and Open Temporary Fixed CCs), which uncertain parameters are considered (Supply, Demand), whether substitutability of blood group types and blood perishability are considered and finally the models' objectives (Minimize Shortage, Wastage, Costs).

Table 4 - Main characteristics of selected papers addressing most of the BSC features to consider in blood collection planning

Article	**Decisions**						**Uncertain Parameters**		**Parameters**		**Objectives:** Minimize		
	Donor Arrival policies	Staff Allocation	Routing	Location-Allocation	Scheduling	Open Temporary Fixed CCs	Supply	Demand	Substitutability	Perishability	Shortage	Wastage	Costs
Zahiri et al. (2013)				√			√	√					√
Jabbarzadeh et al. (2014)				√			√	√					
Alfonso, Augusto & Xie (2015)	√	√	√				√						√
Şahinyazan et al. (2015)			√		√								√
Gunpinar & Centeno (2016)			√		√		√				√		√
Salehi et al. (2017)				√			√	√	√				√
Zahiri & Pishvaee (2017)				√				√	√		√		√
Attari & Jami (2018)		√		√			√	√			√	√	√
Heidari-Fathian & Pasandideh (2018)				√			√	√			√	√	√
Present Work			**√**	**√**	**√**	**√**	**√**	**√**	**√**	**√**	**√**	**√**	**√**

As shown in Table 4, no models are addressing all the decisions concerning blood collection planning. In addition, blood supply and demand uncertainty have been considered in most of the papers as it is an essential environment BSC feature to have a proper blood collection planning. Also, blood perishability and substitutability are considered in a few papers when deciding on blood collection planning. Regarding the models' objectives, minimizing blood wastage and shortage at the lowest possible cost is the most efficient way to ensure a high BSC performance.

Based on the above analysis, the present work considering a multi-echelon existing network aims to combine several BSC challenges into a single framework. One of the present work's main contributions is to develop a model that addresses tactical and operational collection decisions while considering blood products perishability

and blood group types substitutability always ensuring the best patient service level at the lowest costs. Finally, blood potentials and demand uncertainty are to be considered. Using the developed model, the Portuguese BSC blood collection planning will be analysed.

3.5 Chapter Conclusions

Planning collection decisions encompass all hierarchical levels of BSC network: Strategic, Tactical and Operational. Given the importance and difficulty of managing blood flows from donors to patients involved with several challenges, the variety of models proposed over the last 45 years is justified.

The main challenges in planning blood collections are dealing with supply and demand uncertainty as well as considering blood perishability, and the blood group types substitutability. It can be concluded that many approaches focus only on a particular BSC echelon or challenge or limit the blood collection planning to one to three decisions, which keeps literature far from a complete model. Based on this the proposed work aims to be an initial step towards the development of a blood planning collection tool where will be considered demand and supply uncertainty as well as blood perishability and substitutability when making different tactical and operational decisions for a proper blood collection planning with a high quality of patient service level at the lowest cost. The proposed model to address the blood collection planning problem is presented in the next chapter.

Chapter 4: Model Formulation

This chapter aims to present the two-stage stochastic programming model developed to address the above defined blood collection planning problem. Chapters 2 and 3 provide the context on BSC and the necessary knowledge regarding the modelling methodologies covered in the literature, respectively, to develop the optimization model proposed in this chapter. Section 4.1 presents the problem statement and the modelling assumptions. Section 4.2 presents the mathematical formulation and section 4.3 concludes the chapter.

4.1 Problem Statement

This work focuses on the flow of blood between groups of donors and BCs, i.e., from the moment donors decide to donate to the collected blood being processed at BCs and its blood products being delivered to answer blood requests from DZs. Thus, the problem involves assigning mobile and temporary fixed CCs to locations to collect blood from groups of donors allocated to those locations. The goal is to formulate a tactical and operational plan to aid BSC decision-makers regarding blood collection planning considering BSC peculiar properties, as well as the changing willingness and needs of the population. The blood collections planning comprises the first three echelons (Donors, Mobile and Fixed CCs, and BCs) and the early three BSC stages (Collection, Testing and Processing).

The conceptual model under study is shown in Figure 9. When an order arrives at BCs, there is a demand waiting to be fulfilled at DZs. Thus, in advance of blood orders, blood must be collected from groups of donors, denoted by $d \in D$. Blood withdrawals are performed usually at mobile CCs ($m \in M$), but also at fixed CCs ($f \in F$) which are decomposed in temporary fixed CCs and hospitals, and BCs to which each group of donors is allocated. Each BC has its own mobile CCs responsible for blood collection assigned to locations to be closer to groups of donors. It is assumed that the region of interest can be represented by a graph $G = (N, A)$, with nodes (N) and arcs (A) connecting them. The set N of nodes is partitioned into a set B of BCs and a set I of candidate locations for mobile CCs. It is assumed that these candidate locations and groups of donors have been defined a priori.

Regarding the blood collected, as there are different group types of blood due to ABO and RhD group, each blood pack unit is distinguished by blood group type denoted by $g \in G$. After collected, the WB is processed at BCs to obtain blood products ($p \in P$). During the processing stage, there is a percentage of WB that is wasted due to diseases-free testing. This percentage of wastage is considered to have an upper and lower bound. The blood products are stored at BCs until requested from DZs. A minimum inventory level for each blood group type of blood products is fixed. According to ABO compatibility, the substitutability of blood group types is considered to ensure demand fulfilment in case of patient blood group type shortage. The delivery of blood pack units to hospitals follows a FIFO policy, i.e., blood products with shorter remaining shelf-lives are dispatched first. This feature is ensured by considering the wastage of blood pack units as an objective to be minimized.

The decisions to be made include: (1) the routes travelled by mobile CCs (binary variables y_{ijmt}), (2) location-allocation of facilities able to perform blood withdrawals, i.e., the allocation of groups of donors to a specific facility (binary variables x_{dimt}, x'_{dft}, x''_{dbt}), (3) which temporary fixed CCs should be open (binary variables

$openf_{ft}$), (4) the schedule definition for mobile and temporary fixed CCs (continuous variables u_{imt}, u'_{ft} and svm_{imt}), and (5) the quantity of blood to be collected at different facilities, i.e., mobile CCs, fixed CCs, and BCs (continuous variables k_{igt}, k'_{fgt} and k''_{bgt}). The facilities where blood withdrawals are performed have a limited capacity which is assumed to be known in advance. This approach is suitable when BSC decision-makers use existing facilities to collect and stock blood pack units, as is the case of IPST. Similarly, the number of mobile CCs available at each BC is assumed to be known. Moreover, the length of time mobile CCs can be held in a location, and the distance to travel per period is assumed to be limited. The number of hours fixed CCs and BCs have available to perform blood withdrawals is also limited.

After a blood donation, donors must respect the deferral time, which is the fifty-six days that the donor has to wait before making another donation. Thus, mobile, or temporary fixed CCs, after collecting blood from most of the donors respectively allocated, usually do not return to the same location before two months. The model proposed does not consider the necessary deferral time, assuming that groups of donors continually donate.

Providing the best possible service to patients aligned with the lowest costs is the main goal to achieve an optimized system which can be measured by:

- Distance travelled: minimizing the distance travelled by mobile CCs and vehicles which transport blood;
- Blood shortage: minimizing the shortage of blood pack units;
- Blood wastage: minimizing the wastage of outdated blood pack units;
- ABO compatibility: minimizing the substitutability of blood group types;
- Blood transhipment: minimizing the transhipment of blood pack units between BCs;
- Open temporary fixed CCs: minimizing the temporary fixed CCs to open.

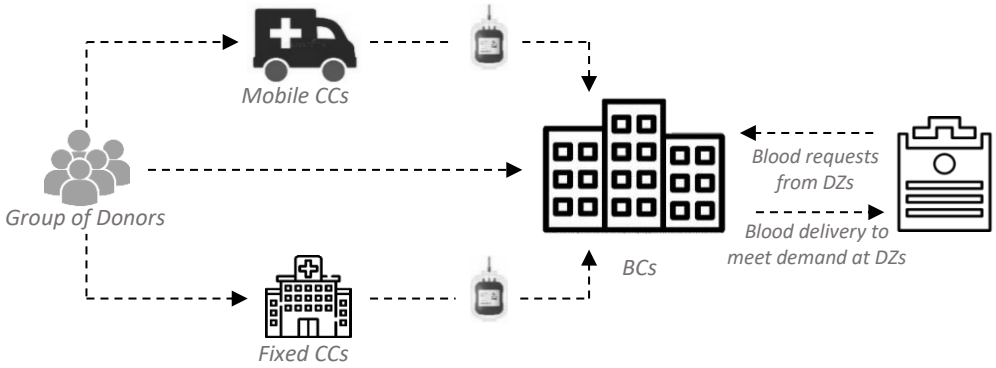

Figure 9 - Problem flows

4.2 Mathematical Formulation

In this section the mathematical formulation of the model is presented. The model is based on Gunpinar & Centeno (2016) for VRP decisions and Zahiri et al. (2013) for location-allocation decisions. The proposed model differs from these models since both decisions are considered simultaneously in the same model, ensuring the BSC integrability for the two echelons involved, Donors and Mobile CCs. Also, neither the two works address

blood perishability, nor blood group types substitutability. These perishability and substitutability considerations are based on Dillon, Oliveira, & Abbasi (2017) for the inventory management of the BSC.

In subsection 4.2.1, the model is characterized. Subsection 4.2.2 introduces sets and subsets, and subsection 4.2.3 presents the model parameters. Then, subsection 4.2.4 introduces the decision variables and, finally, the objective function and constraints are presented in subsection 4.2.5.

4.2.1 Uncertainty Treatment Model Approach

The model developed considers a two-stage stochastic programming approach to make realistic decisions regarding supply and demand uncertainty. In the first stage, decisions which do not depend on parameter stochasticity are made, while decisions depending on uncertainty are delayed for the second stage at a specific cost. This cost is assigned to the recourse activities taken to ensure the feasibility of the second stage problem.

This two-stage stochastic programming approach is represented in Figure 10, where are identified the main constraints, formulated below, as well as the decisions taken.

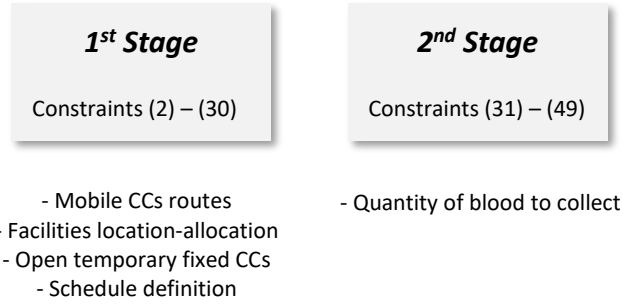

Figure 10 - Two-stage stochastic programming approach

As mentioned previously, the problem integrates the tactical and operational levels of decision regarding blood collection planning. The first stage's output is mobile CCs routes, location-allocation of facilities, temporary fixed CCs to open, and the schedule definition. The first three decisions regard the tactical level, and the latter relates to the operational level. To inform donors, the schedule of blood withdrawals must be known in advance. Thus, these decisions are made before uncertainty is realised since blood donations are unknown until the arrival of donors at any facility. Stage two outputs the quantity of blood of different group types to collect to fulfil blood demand. These decisions regarding which products and quantities to order belong to the operational level. The model final results consider a robust set of decisions that accounts for all uncertainties considered.

4.2.2 Sets and Subsets

The following sets are defined:

$i, j, b, b', h \in N$	Set of BCs locations and candidate locations for mobile CCs
$f \in F$	Set of fixed CCs locations
$m \in M$	Set of mobile CCs
$d \in D$	Set of groups of donors
$t, t' \in T$	Set of time periods

$p \in P$	Set of WB and derived products
$g, g' \in G$	Set of blood group types
$s \in S$	Set of scenarios

Together with the following subsets:

$i, j \in I$	Candidate locations for mobile CCs
$b, b' \in B$	BCs locations
$p \in P^{dp}$	Derived WB products
$f \in F^{H}$	Hospitals locations
$f \in F^{T}$	Temporary fixed CCs locations

4.2.3 Parameters

Parameters are required as model input data:

VRP Parameters

$dist_{ij}$	Distance from location i to location j
$distfb_{fb}$	Distance from location f to location b
π_{ib}	Correspondence matrix of which locations i belong to BC b
π'_{fb}	Correspondence matrix of which fixed CC at location f transport blood to BC b
t_{mb}	Correspondence matrix of which mobile CC m belong to BC b

Coverage Parameters

ri_{di}	Distance between the centre of a group of donors d and location i
ri_0	Coverage radius of mobile CCs (if $ri_{di} \leq ri_0$, d is covered by i)
rf_{df}	Distance between the centre of a group of donors d and location f
rfH_o	Coverage radius of hospitals (if $rf_{df} \leq rfH_o$, d is covered by $f \in F^H$)
rfT_o	Coverage radius of temporary fixed CCs (if $rf_{df} \leq rfT_o$, d is covered by $f \in F^T$)
rb_{db}	Distance between the centre of a group of donors d and location b
rb_0	Coverage radius of BCs (if $rb_{db} \leq rb_0$, d is covered by b)

Scheduling Parameters

$travelt_{ij}$	Travel time from location i to location j
$departure$	Mobile CCs departure time from BCs
$arrival$	Mobile CCs arrival time to BCs

Inventory Parameters

$inil_{bpg}$	Initial inventory level of blood product p of group type g in each BC b
$Imin_{bpg}$	The minimum stock level of blood product p of group type g in each BC b
β_p	Production factor of blood product p

SL_p	The maximum shelf-life of blood product p
σ^-	Lower bound factor for WB sample wastage
σ^+	Upper bound factor for WB sample wastage
dem_{bpgst}	Demand for blood product p of group type g at BC b in scenario s for time period t
pot_{dgst}	Expected blood potentials of group type g that group of donors d donate in scenario s in time period t
$\Delta_{g'g}$	ABO group compatibility matrix ($\Delta_{g'g} = \begin{cases} 1, & \text{if demand for blood type } g' \text{ may be met by type } g \\ 0, & \text{otherwise} \end{cases}$)
$\nabla_{g'g}$	ABO group substitution priority matrix

Resource Parameters

Qm	Mobile CCs capacity
Qv	The capacity of vehicles which transport blood product units from fixed CCs and between BCs
Qb	BCs capacity
$Hmax$	The maximum length of time a mobile CC can be held in a location
$Dmax$	The maximum distance a mobile CC can travel in each period
$OpenHf$	Number of hours a fixed CC is available to perform blood withdrawals
$OpenHb$	Number of hours a BC is available to perform blood withdrawals

Cost Parameters

$transpC$	Cost of transporting blood pack units per km
$wstC$	Cost per blood product unit wasted
$stgC$	Cost per blood product unit shorted
$trspC_p$	Cost per blood product unit transhipped
$openfC$	Cost per temporary fixed CC open

Objective Function Parameters

θ^1	Weight for distance travelled cost
θ^2	Weight for wasted units cost
θ^3	Weight for shorted units cost
θ^4	Weight for ABO substitutions cost
θ^5	Weight for transhipments cost
θ^6	Weight for opening temporary fixed CCs cost
$ps(s)$	Probability of scenario s

4.2.4 Decision Variables

The model includes decision variables as well as auxiliary variables. For a stochastic programming model, the decision variables can be divided into the first stage (or here-and-now) and second stage (or recourse) decision variables.

Decision Variables

These variables concern the mobile CC routes to collect blood from groups of donors and the location-allocation of facilities where blood withdrawals are performed. There also exist variables concerning which temporary fixed CCs to open per period, and the schedule definition for mobile and temporary fixed CCs to perform blood withdrawals. All the former variables correspond to first-stage variables since these decisions need to be made regardless of the scenario. Finally, the last three sets of variables concern the quantity of blood pack units to collect in the different collection points depending on the scenario.

y_{ijmt} $\begin{cases}1, & \text{if mobile CC } m \text{ travels from location } i \text{ to location } j \text{ in time period } t \\ 0, & \text{otherwise}\end{cases}$

x_{dit} $\begin{cases}1, & \text{if a group of donors } d \text{ is assigned to location } i \text{ in period } t \\ 0, & \text{otherwise}\end{cases}$

x'_{dft} $\begin{cases}1, & \text{if a group of donors } d \text{ is assigned to a fixed CC } f \text{ in period } t \\ 0, & \text{otherwise}\end{cases}$

x''_{dbt} $\begin{cases}1, & \text{if a group of donors } d \text{ is assigned to a BC } b \text{ in period } t \\ 0, & \text{otherwise}\end{cases}$

$openf_{ft}$ $\begin{cases}1, & \text{if a temporary fixed location } f \in F^T \text{ is open in period } t \\ 0, & \text{otherwise}\end{cases}$

u_{imt} Visit duration of mobile CC m in location i in time period t

u_{ft} Amount of time a temporary fixed location $f \in F^T$ is open in time period t

svm_{imt} The time mobile CC m starts servicing location i in time period t

k_{imgst} Quantity of blood pack units of group type g collected at location i by mobile CC m in scenario s in time period t

k'_{fgst} Quantity of blood pack units of group type g collected by fixed CC f in scenario s in time period t

k''_{bgst} Quantity of blood pack units of group type g collected by BC b in scenario s in time period t

Auxiliary Variables

These variables are used to control the stability of the BSC system and support the decisions. The first four variables are "here and now" decisions made before the blood supply and demand uncertainty realization. The remaining variables are recourse decisions made after the uncertainty is realized.

z_{bmt} $\begin{cases}1, & \text{if mobile CC } m \text{ is selected with a team of BC } b \text{ to collect blood in time period } t \\ 0, & \text{otherwise}\end{cases}$

l_{imt} $\begin{cases}1, & \text{if location } i \text{ is visited by mobile CC } m \text{ in time period } t \\ 0, & \text{otherwise}\end{cases}$

fl_{ijt} Number of arcs on the path from BC b to arc (i, j) in the optimal tour per time period

gl_{ijt} Arc current from BC b to arc (i, j) in the optimal tour per time period

$iftrans_{fst}$ $\begin{cases}1, & \text{if blood product units are transported from fixed CC } f \text{ to BC } b \text{ in scenario } s \text{ in time period } t \\ 0, & \text{otherwise}\end{cases}$

col_{bgst} Quantity of blood pack units of group type g collected for BC b in scenario s in time period t

$prod_{bpgst}$ Quantity of blood pack units of blood product p of group type g produced in BC b in scenario s in time period t

$v_{bpgt'st}$ Inventory level at BC b of blood product p of group type g collected in time period t' in scenario s at the end of period t

$del_{bpgg't'st}$ Quantity of blood pack units of blood product p of group type g collected in period t' delivered by BC b to satisfy the blood demand of group type g' in scenario s at the end of time period t

$trsp_{b'bpgt'st}$ Quantity of blood product pack units p of group type g collected in time period t' transhipped from BC b' to BC b in scenario s at period t

$iftrsp_{b'bst}$ $\begin{cases} 1, & \text{if blood product units are transhipped from BC } b' \text{ to BC } b \text{ in scenario } s \text{ in time period } t \\ 0, & \text{otherwise} \end{cases}$

wst_{bpgst} Quantity of blood pack units of blood product p of group type g wasted in BC b because of outdatedness in scenario s at the end of time period t

stg_{bpgst} Quantity of blood pack units of blood product p of group type g lacking in BC b in scenario s at the end of time period t

4.2.5 Objective Function and Constraints

In this section, a mathematical model for the blood collection planning is presented while considering the complexities of blood products perishability and substitutability between blood group types. The model is a two-stage stochastic programming model where supply and demand uncertainty are both modelled as scenario-based. First, a mixed integer non-linear programming (MINLP) formulation is presented. Due to the complexity of this non-linear model, the non-linear constraints are linearized.

As stated, the objective function has emerged from how to provide the best possible service to patients while ensuring the lowest costs. Therefore, the model seeks to minimize the costs associated with: the distance travelled in kilometres between collection points; the blood products units shortage and wastage; the blood products units substitutability between blood group types; the blood products units transhipment between BCs; and the opening of temporary fixed CCs to perform blood withdrawals. The objective function is formulated in expression (1).

$$minimize\ OverallCost = \theta^1.Ind^1 + \theta^2.Ind^2 + \theta^3.Ind^3 + \theta^4.Ind^4 + \theta^5.Ind^5 + \theta^6.Ind^6 \quad (1)$$

$$Ind^1 = transpC\left(\sum_{i,j,m,t} dist_{ij}.y_{ijmt} + \sum_{i,j,m,s,t} distfb_{fb}.iftrans_{fst}.ps(s)\right) \quad (1a)$$

$$Ind^2 = wstC.\sum_{b\in B,p,g,s,t} wst_{bpgst}.ps(s) \quad (1b)$$

$$Ind^3 = stgC.\sum_{b\in B,p\in P^{dp},g,s,t} stg_{bpgst}.ps(s) \quad (1c)$$

$$Ind^4 = stgC.\sum_{b\in B,p\in P^{dp},g,g',t',s,t} del_{bpgg't'st}.\nabla_{g'g}.ps(s) \quad (1d)$$

$$Ind^5 = \left(\sum_{b,b' \in B, p \in P^{dp}, g, t', s, t} trspC_p . trsp_{b'bpgt'st} . ps(s) \right. \quad (1e)$$
$$\left. + transpC . \sum_{b,b' \in B, s, t} iftrsp_{b'bst} . dist_{bb'} . ps(s) \right)$$

$$Ind^6 = openfC . \sum_{f \in F^T, t} openf_{ft} \quad (1f)$$

The objective function (1) minimizes costs weighted by six parameters - $\theta^1, \theta^2, \theta^3, \theta^4, \theta^5, \theta^6$. The first term – indicator Ind^1 corresponds to the cost in kilometres of the distance travelled by mobile CCs during their routes through locations to perform blood withdrawals, and of the distance travelled by vehicles responsible for transporting blood from fixed CCs to BCs are given by $dist_{ij} \, . \, y_{ijmt}$ and $distfb_{fb} . iftrans_{fst}$ respectively. The second term – indicator Ind^2 depicts wastage disposal costs regarding WB which is not processed and the wastage costs of outdated blood pack units (wst_{bpgst}). The third term – indicator Ind^3 relates to the cost per blood pack units shorted to fulfil blood demand (stg_{bpgst}). The fourth term – indicator Ind^4 regards the cost per blood pack units of different blood group types used to satisfy compatible blood products pack units demand ($del_{bpg'gt'st} \, . \, \nabla_{g'g}$). This substitutability is medically considered as poor quality of service (Katsaliaki, 2008). The fifth term – indicator Ind^5 relates to the opportunity to tranship blood from a BC with excess blood to a BC with lack of blood which is given by the cost per blood product units transhipped from other BC ($trsp_{b'bpgt'st}$) and the cost in kilometres of the distance travelled between these BCs ($iftrsp_{b'bst} . dist_{bb'}$). Finally, the last term – indicator Ind^6 relates to the cost per temporary fixed CCs ($openf_{ft}$) open. The indicators costs which are not related to distance travelled are considered perceived costs as they are not possible to be quantified. Using the weights $\theta^1, \theta^2, \theta^3, \theta^4, \theta^5$ and θ^6 allows to control the relative importance of each indicator. To address the uncertainty of blood supply and demand, the probability of the scenarios ($ps(s)$) is considered for the indicators which depend on uncertainty.

VRP Constraints

This first group of constraints regards the mobile CC routes and limitations to their assignment to locations.

$$\sum_{j \in N} y_{ijmt} = l_{imt} \qquad \forall i \in I, i \neq j; m; t \qquad (2)$$

$$\sum_{m} l_{imt} \leq 1 \qquad \forall i \in I; t \qquad (3)$$

$$\sum_{j \in I} y_{bjmt} = z_{bmt} \qquad \forall b \in B; m; t \qquad (4)$$

$$\sum_{i \in N} y_{ihmt} - \sum_{j \in N} y_{hjmt} = 0 \qquad \forall h \in I; m; t \qquad (5)$$

$$\sum_{i \in I} y_{ibmt} = z_{bmt} \qquad \forall b \in B; m; t \qquad (6)$$

$$y_{bjmt} \leq \pi_{jb} \qquad \forall b \in B; j \in I; m; t \qquad (7)$$

$$y_{ibmt} \leq \pi_{ib} \qquad \forall b \in B; i \in I; m; t \qquad (8)$$

$$\sum_{m} y_{bbmt} = 0 \qquad \forall b \in B; t \qquad (9)$$

$$z_{bmt} \leq t_{mb} \qquad \forall b \in B; m; t \qquad (10)$$

$$\sum_{(i,j)} y_{ijmt}.dist_{ij} \leq Dmax \qquad \forall i \neq j; m; t \qquad (11)$$

Constraints (2) guarantee that if there is an arc leaving node i by mobile CC m in period t, then node i must have been visited. Constraints (3) force each location to be visited no more than once each period. These constraints are necessary because it makes no sense two mobile CCs visit the same location simultaneously or even one after the other in time period t due to set up time before starting to perform blood withdrawals.

Constraints (4)-(6) are arc flow constraints for each time period t indicating that if a mobile CC has at least one location to visit then, it must leave from a BC b, after visiting a location i it has to leave for another destination, and, finally, it must arrive at the BC b. Constraints (4) also define that if there is an arc leaving from BC b then there is a mobile CC with a team from BC b to be used.

Constraints (7) and (8) ensure that if a mobile CC m leaves or arrives from or to BC b, mobile CC must travel to or from a location which belongs to BC b coverage area, respectively. These constraints are due to the blood demand which arrives at a BC b which must be met by blood collected at locations within BC b coverage area. Constraints (9) forbids tours between BCs. Since each BC has its own mobile CCs then constraints (10) ensure that a mobile CC m leaves only from its respective BC. Constraints (11) limit the total travel distance of mobile CC m in each period.

$$\sum_{b \in B} \sum_{j \in I} fl_{bjt} = \sum_{m} \sum_{j \in I} l_{jmt} \qquad Vt \qquad (12)$$

$$\sum_{j \in N} fl_{jit} - \sum_{j \in I} fl_{ijt} = \sum_{m} l_{imt} \qquad Vi \in I; i \neq j; t \qquad (13)$$

$$fl_{ijt} \leq (|I| - 1). \sum_{m} y_{ijmt} \qquad Vi, j \in I; i \neq j; t \qquad (14)$$

$$fl_{bjt} \leq |I|. \sum_{m} y_{bjmt} \qquad Vb \in B; j \in I; t \qquad (15)$$

Constraints (12)-(15) eliminate possible subtours by applying the single commodity flow formulation proposed by Gavish & Graves (1978). By sending flow from the BCs and leaving one unit at each location, connectivity between BCs and locations is ensured, thus preventing subtours. Constraints (12) state that the number of units of flow leaving the set of BCs is the number of locations j visited in each period. Constraints (13) ensure that one unit of flow is left at each visited location. Constraints (14) and (15) define upper bounds for the flow on each arc.

$$gl_{bit} \leq b. \sum_{m} y_{bimt} \qquad Vb \in B; i \in I; t \qquad (16)$$

$$gl_{ibt} \leq b. \sum_{m} y_{ibmt} \qquad Vb \in B; i \in I; t \qquad (17)$$

$$\sum_{j \in N} gl_{jit} - \sum_{j \in N} gl_{ijt} = 0 \qquad Vi \in I; i \neq j; t \qquad (18)$$

$$gl_{ijt} \leq |I|. \sum_{m} y_{ijmt} \qquad Vi, j \in I; i \neq j; t \qquad (19)$$

Constraints (16)-(19) define the arc-current formulation proposed by Bektas, Gouveia, & Santos (2020), which is used to ensure that mobile CCs return to their original BC at the end of their route. Constraints (16) and (17) specify that the current of the arcs leaving and entering a BC b is equal to b, respectively. Constraints (18) relate to flow conservation and ensure that the current of an arc that belongs to a BC circuit is the same as of that BC. Finally, constraints (19) define upper bounds on the currents for arcs between locations and state the link between gl_{ijt} and y_{ijmt} variables.

Coverage Constraints

Coverage constraints deal with allocating groups of donors to locations where blood withdrawals are performed, ensuring those allocations are possible.

$$x_{dit}.ri_{di} \leq ri_0.\sum_m l_{imt} \qquad \forall d; i \in I; t \qquad (20)$$

$$x'_{dft}.rf_{df} \leq rfH_0 \qquad \forall d; f \in F^H; t \qquad (21)$$

$$x''_{dbt}.rb_{db} \leq rb_0 \qquad \forall d; b \in B; t \qquad (22)$$

$$x'_{dft}.rf_{df} \leq rfT_0 * openf_{ft} \qquad \forall d; f \in F^T; t \qquad (23)$$

$$\sum_{i \in I} x_{dit} + \sum_f x'_{dft} + \sum_{b \in B} x''_{dbt} \leq 1 \qquad \forall d; t \qquad (24)$$

Constraints (20)-(24) indicate coverage restrictions. Constraints (20) ensure that a group of donors is allocated to location i if the group of donors is within the coverage radius and if the location i is visited by a mobile CC. Constraints (21) and (22) relate to allocating groups of donors within the coverage radius of hospitals and BCs, respectively. These facilities are available every time period to perform blood withdrawals. Constraints (23) set the allocation of groups of donors to temporary fixed CCs which are open. To guarantee that group of donors donate blood at the nearest location, constraints (24) assure that in each time period, each group of donors only donate to one of the donation locations, namely the closest one.

Schedule Constraints

Schedule constraints build the mobile CCs visits schedule, i.e., the time mobile CC m starts to collect at location i in time period t and the end time of the visit.

$$svm_{bmt} \geq departure.\sum_j y_{bjmt} \qquad \forall b \in B; m; t \qquad (25)$$

$$svm_{jmt} \geq svm_{bmt} + travelt_{bj} - BigM.(1 - y_{bjmt}) \qquad \forall b \in B; j \in I; m; t \qquad (26)$$

$$svm_{jmt} \geq svm_{imt} + u_{imt} + travelt_{ij} - BigM.(1 - y_{ijmt}) \qquad \forall (i,j) \in I, i \neq j; m; t \qquad (27)$$

$$svm_{imt} + u_{imt} + travelt_{ib} - BigM.(1 - y_{ibmt}) \leq arrival \qquad \forall i \in I; b \in B; m; t \qquad (28)$$

Constraints (25) set the time a mobile CC leaves the BC to travel to locations. Constraints (26) determine that the collections starting time at the first location visited depends on the travel duration from the BC. Constraints (27) establish the relationship between the mobile CC departure time from a location and the immediate successor location. A mobile CC's arrival time to a location must be after the mobile CC arrival time at the previous location plus its stay duration and travel time between both locations. Constraints (28) define the completion time for blood withdrawals.

Blood Collection Constraints

This set of constraints controls the blood collected in the different facilities which perform blood withdrawals.

$$u_{imt} \leq Hmax.l_{imt} \qquad \forall i \in I; m; t \qquad (29)$$

$$u'_{ft} \leq OpenHf.openf_{ft} \qquad \forall f \in F; m; t \qquad (30)$$

$$\sum_d pot_{dgst}.x_{dit}.u_{imt} \geq k_{imgst} \qquad \forall i \in I; g; m; s; t \qquad (31)$$

$$\sum_d pot_{dgst}.x'_{dft}.u'_{ft} \geq k'_{fgst} \qquad \forall f \in F^T; g; s; t \qquad (32)$$

$$\sum_d pot_{dgst}.OpenHf.x'_{dft} \geq k'_{fgst} \qquad \forall f \in F^H; g; s; t \qquad (33)$$

$$\sum_d pot_{dgst}.OpenHb.x''_{dbt} \geq k''_{bgst} \qquad \forall b \in B; g; s; t \qquad (34)$$

$$col_{bgst} = \sum_{i \in I} \sum_m k_{imgst}.\pi_{ib} + \sum_f k'_{fgst}.\pi_{fb} + k''_{bgst} \qquad \forall b \in B; g; s; t \qquad (35)$$

$$\sum_{i \in I} \sum_g k_{imgst} \leq Qm \qquad \forall m; s; t \qquad (36)$$

$$\sum_g k'_{fgt} \leq iftrans_{fst}.Qv \qquad \forall f; s; t \qquad (37)$$

The blood collected by mobile CCs depends on the duration of stay at the location assigned, and if groups of donors are allocated to the respective location. The blood collected by temporary fixed CCs depends on the duration the facility is open to collect blood and if groups of donors are allocated to the location. Hospitals and BCs only depend on the availability to perform blood withdrawals. Constraints (29) limit the number of hours a mobile can stay at location i in time period t if the location is visited and constraints (30) limit the number of hours a temporary fixed CC is open to perform blood withdrawals if the facility is open in time period t. Constraints (31)-(34) define the amount of blood pack units of each blood group type that can be collected by mobile CCs, fixed CCs and BCs from the groups of donors allocated to these facilities where blood withdrawals are performed in time period t in scenario s, respectively. Once blood orders arrive at BCs, the blood collected at the different locations must be assigned to the BC, which covers those locations to fulfil blood demand. Thus, constraints (35) define the total blood pack units of group type g collected from mobile CCs, fixed CCs, and the BC itself which belong to the BC's cover region in scenario s in time period t. Constraints (36) and (37) are capacity constraints for mobile and fixed CCs, respectively, in each time period and per scenario s.

Blood Processing Constraints

This set of constraints deals with the production of blood products through blood processing.

$$prod_{bpgst} \leq \beta_p.col_{bgst} \qquad \forall b \in B; p \in P^{dp}; g; s; t \qquad (38)$$

$$wst_{b"WB"gst} \geq \sigma^-.col_{bgst} \qquad \forall b \in B; g; s; t \qquad (39)$$

$$wst_{b"WB"gst} \leq \sigma^+.col_{bgst} \qquad \forall b \in B; g; s; t \qquad (40)$$

$$\frac{prod_{bpgst}}{\beta_p} + wst_{bWBgst} = \beta_p.col_{bgst} \qquad \forall b \in B; p \in P^{dp}; g; s; t \qquad (41)$$

When collected, blood is referred to as WB. After collected, the WB must be processed into derived blood products. The WB available at a BC in scenario s in time period t is decomposed into derived blood products according to a given production ratio, as constraints (38) define. Before processing, blood must be tested to ensure the donor is diseases free. As in this testing stage the blood sample tested is wasted, constraints (39) ensure minimum blood wastage from the WB collected. Constraints (40) model the waste inherent to the inefficiencies of the production process imposing a maximum allowed wastage. Constraints (41) assure the flow conservation of WB in each BC. The constraints state that all WB collected arriving at the BC from the respective cover region locations is either processed or discarded.

Inventory Constraints

Finally, this group of constraints defines inventory levels, considering upper and lower bounds.

$$v_{bpgtst} = inil_{bpg} + prod_{bpgst} - \sum_{g'} del_{bpgg'tst} \cdot \Delta_{g'g} + \sum_{b' \in B} trsp_{b'bpgtst} - \sum_{b\prime \in B} trsp_{bb\prime pgtst} \quad \forall b \in B; b' \neq b; p \in P^{dp}; g; s; t = 1 \quad (42)$$

$$v_{bpgtst} = prod_{bpgst} - \sum_{g'} del_{bpgg'tst} \cdot \Delta_{g'g} + \sum_{b' \in B} trsp_{b'bpgtst} - \sum_{b\prime \in B} trsp_{bb\prime pgtst} \quad \forall b \in B; b' \neq b; p \in P^{dp}; g; s; t > 1 \quad (43)$$

$$v_{bpgt\prime st} = v_{bpgt\prime s(t-1)} - \sum_{g'} del_{bpgg't'st} \cdot \Delta_{g'g} + \sum_{b' \in B} trsp_{b'bpgt'st} - \sum_{b' \in B} trsp_{bb'pgt'st} - v_{bpg(t-SL)s(t-1)} \quad \forall b \in B; b' \neq b; p \in P^{dp}; g; t - SL \leq t' < t; s; t \quad (44)$$

$$\sum_{t'=t-SL}^{t} v_{bpgt\prime st} \geq Imin_{bpg} \quad \forall b \in B; p \in P^{dp}; g; s; t \quad (45)$$

$$\sum_{p \in P^{dp}} \sum_{g} \sum_{t'=t-SL}^{t} v_{bpgt\prime st} \leq Qb \quad \forall b \in B, s; t \quad (46)$$

$$\sum_{t'=t-SL}^{t} \sum_{g'} del_{bpgg\prime t\prime st} \cdot \Delta_{g\prime g} = dem_{bpgst} + stg_{bpgst} \quad \forall b \in B; p \in P^{dp}; g; s; t \quad (47)$$

$$\sum_{t'=t-SL} v_{bpgt\prime s(t-1)} = wst_{bpgst} \quad \forall b \in B; p \in P^{dp}; g; s; t \quad (48)$$

$$\sum_{p \in P^{dp}, g, t, t\prime} trsp_{bb\prime pgt\prime st} \leq iftrsp_{b'bst} . Qtrsp \quad \forall (b, b') \in B; s; t \quad (49)$$

Constraints (42) and (49) model are inventory conservation constraints for each BC in every time period per scenario s. Constraints (42) and (43) define, for the first and remaining time periods, respectively, the inventory level of blood products pack units of each group type. These pack units are produced, delivered, and transhipped between BCs in the same time period and per scenario s to satisfy the demand of a group type or a compatible one. Constraints (44) define the inventory level at BCs based on the inventory from the previous period, the transhipment of blood pack units between BCs and the delivery of blood products pack units of each blood group type. The products packs units were collected in time period t' at the end of the present time period to satisfy the demand of a blood group type or a compatible one in scenario s. The age of these blood products pack units

must be within the respective blood product shelf-life since outdated units are discarded from the inventory. Constraints (45) and (46) ensure a minimum and maximum stock level at BCs. If the blood delivered by BCs does not satisfy all the blood product demand, there is a shortage of the blood packs units, modelled by constraints (47). Constraints (48) define that the blood not used before the end of its shelf-life is wasted, i.e. there is a wastage associated with outdated blood pack units. Finally, constraints (49) ensure the vehicle capacity constraints when transhipping blood products units between BCs.

Linearization of the non-linear constraints

Constraints (31) and (32), which model the amount of blood collected by mobile CCs at the locations assigned or at temporary fixed CCs, respectively, can be replaced by a set of linear constraints as follows:

$$\sum_d pot_{dgst}.e_{dimt} \geq k_{imgst} \qquad \forall i \in I; g; m; s; t \qquad (50)$$

$$e_{dimt} \leq u_{imt} \qquad \forall i \in I; d; m; t \qquad (51)$$

$$e_{dimt} \leq x_{dit}.Hmax \qquad \forall i \in I; d; m; t \qquad (52)$$

$$e_{dimt} \geq u_{imt} - Hmax.(1 - x_{dit}) \qquad \forall i \in I; d; m; t \qquad (53)$$

$$\sum_d pot_{dgst}.e'_{dft} \geq k'_{fgst} \qquad \forall f \in F^T; g; s; t \qquad (54)$$

$$e'_{dft} \leq u'_{ft} \qquad \forall f \in F^T; d; t \qquad (55)$$

$$e'_{dft} \leq OpenHf.x'_{dft} \qquad \forall f \in F^T; d; t \qquad (56)$$

$$e'_{dft} \geq u'_{ft} - OpenHf.(1 - x'_{dft}) \qquad \forall f \in F^T; d; t \qquad (57)$$

The set of constraints (50)-(53) and (54)-(57) are equivalent to non-linear constraints (31) and (32), respectively, where $u_{imt}.x_{dit} = e_{dimt}$ and $u'_{ft}.x'_{dft} = e'_{dft}$. When any group of donors is allocated to a location, the blood collected by mobile CCs depends on the duration of stay ($x_{dit} = 1$, then $u_{imt} \geq 0$) and the blood collected by temporary fixed CCs depends on the duration the facility is open ($x'_{dft} = 1$, then $u'_{ft} \geq 0$). When any group of donors is assigned, there is no duration of stay because mobile CC is not allocated to the location ($x_{dit} = 0$, then $u_{imt} = 0$) or there is no available time for blood withdrawals at temporary fixed CC because these are not opened ($x'_{dft} = 0$, then $u'_{ft} = 0$).

4.3 Chapter Conclusion

In this chapter, the problem under study is formalized, and a MINLP model is formulated and linearized. This model is proposed to aid blood collection planning by considering five decisions: mobile CCs routes, location-allocation of facilities, i.e., allocation of groups of donors to different facilities which perform blood withdrawals, which temporary fixed CCs to open, the schedule definition for mobile and temporary fixed CCs to perform blood withdrawals, and the quantity of blood to collect from groups of donors. Thus, these decisions encompass both tactical and operational level. Furthermore, the objective of reducing costs along with a set of constraints which depict the BSC characteristics. A two-stage stochastic programming approach is used to tackle blood supply and demand uncertainty.

The following chapter identifies the assumptions made regarding the data used. It describes the data collection and treatment carried out to apply the proposed model to the IPST blood collection planning.

Chapter 5: Data Collection and Treatment

In this chapter, the data collection and treatment procedures are introduced. The assumptions adopted are present in section 5.1, including data which is not available by IPST. Section 5.2 describes data collection and treatment procedures required to transform data into parameters, and section 5.3 presents the chapter's conclusions.

5.1 Assumptions and Limitations

This section presents the assumptions and limitations considered to estimate the model inputs from the available annual data regarding 2019. Due to a lack of information regarding possible candidate locations for mobile and temporary fixed CCs, these were generated randomly. However, the number of locations generated was not close to reality due to the proposed model's dimensioning issues and complexity. Regarding travel time and distance when mobile CCs leave BCs to perform blood collections or when vehicles tranship blood products between BCs, Google Maps functionalities were used to calculate this information. Travel times are assumed to be independent of traffic throughout the year. Moreover, when locating a mobile or temporary fixed CC, IPST tries to draw specific targets' attention. Due to lack of information, groups of donors are defined with centroids generated randomly.

To support the IPST blood collection plan during the year, a 7-day planning horizon is analysed. Due to the importance of having a daily schedule for mobile CCs, a minimum time period of one day was considered. Unfortunately, due to the complexity of the model and the instances' dimension, there is no possibility of planning more than 7 days and getting reasonable results in an acceptable time (e.g., five hours of computational time). Although a 7-days planning horizon does not encompass the consideration of the RBC shelf-life of 42 days, the platelets shelf-life is covered, allowing to assess the model's perishability consideration.

Finally, to ensure a good service level to patients, performance indicators are assumed to have associated costs. The transportation cost regards the transportation of blood pack units between echelons. The wastage cost is associated with an unethical decision to avoid. The shortage cost and substitution cost relate to the non-compliance with a quality patient service level. Finally, the costs of transhipment and opening temporary fixed CCs regards perceived costs for IPST relating to the self-sufficiency of BCs and of reaching more groups of donors at a non-efficient way due to the need for equipment transportation and installation, respectively. All these costs are assumed to remain constant throughout the planning horizon.

5.2 Data Collection and Treatment Procedures

The dissertation aims to propose a blood collection plan to meet demand and minimize waste using a scenario based on 2019 annual data from the Portuguese BSC managed by IPST. The annual data is deducted for daily data to be used in the 7-day planning horizon. Therefore, model inputs are generated by collecting and treating relevant data regarding the Portuguese BSC. The data collection procedures applied include:

1. An analysis of historical collection and transfusion records from 2019 (the most recent available records) to develop blood potentials and demand forecasts for the planning period;

2. The use of Google Maps to estimate parameters for which historical data is not available.

In subsection 5.2.1, the collection area for mobile and temporary fixed CCs is defined. Subsection 5.2.2 defines the group of donors locations and their coverage radius, and subsection 5.2.3 presents the resources, schedule, and inventory parameters considered. In subsection 5.2.4, the considered blood products and blood group types are presented, and in subsection 5.2.5 and subsection 5.2.6 the blood potentials and demand definition are explained, respectively. Finally, subsection 5.2.7 explains the considered costs.

5.2.1 Collection points

IPST is responsible for collecting blood from donors, preparing the blood pack units, and delivering them at DZs. Thus, IPST locates mobile or temporary fixed CCs to collect sufficient blood to meet demand. IPST's strategy is to locate mobile and temporary fixed CCs near the population to increase awareness for blood donation. Examples of candidate locations for CCs are near universities, shopping centres, areas with several companies, health centres of the parishes, i.e., in crowded locations.

Given the unavailability of IPST information regarding the usual mobile and temporary fixed CCs candidate locations to perform blood collection, random locations were generated per Portuguese municipality. Thus, by considering each municipality centre's coordinates and their area, a circular area was assumed for each municipality. The random candidate locations for mobile and temporary fixed CCs per municipality were generated inside the respective circular area. After generating a large number of random candidate locations for mobile and temporary fixed CCs, the total number of locations resulted in a large dimension instance that could not be solved with the complex model dealing with most of the BSC challenges. To reduce the instance size, an activity level from 1 to 5 was set depending on each Portugal municipality inhabitants' number (Figure 11.a) and 11.b)). The choice of municipalities to test in the model are those with an activity level of 3 to 5 but ensuring the same number of municipalities per decentralized national centre (Figure 11.c)). For each municipality with an activity level of 3 or 4, only one candidate location for mobile CC was generated. In contrast, two candidate locations were generated for municipalities with an activity level of 5. Regarding temporary fixed CCs, only one candidate location was generated for each municipality considered, since temporary fixed CCs are more common than hospitals but less common than mobile CCs. The fixed CC locations considered are Portuguese hospitals where blood withdrawals can be performed. The information regarding the hospitals prepared to perform blood withdrawals is available in IPST's annual report of the Portuguese hemovigilance system corresponding to 2019.

Figure 11.d) illustrates the different collections points considered in the model, which are candidate locations for mobile and temporary fixed CCs – orange and blue bullets, respectively. The figure also illustrates the selected hospitals and BCs locations – yellow and red bullets, respectively.

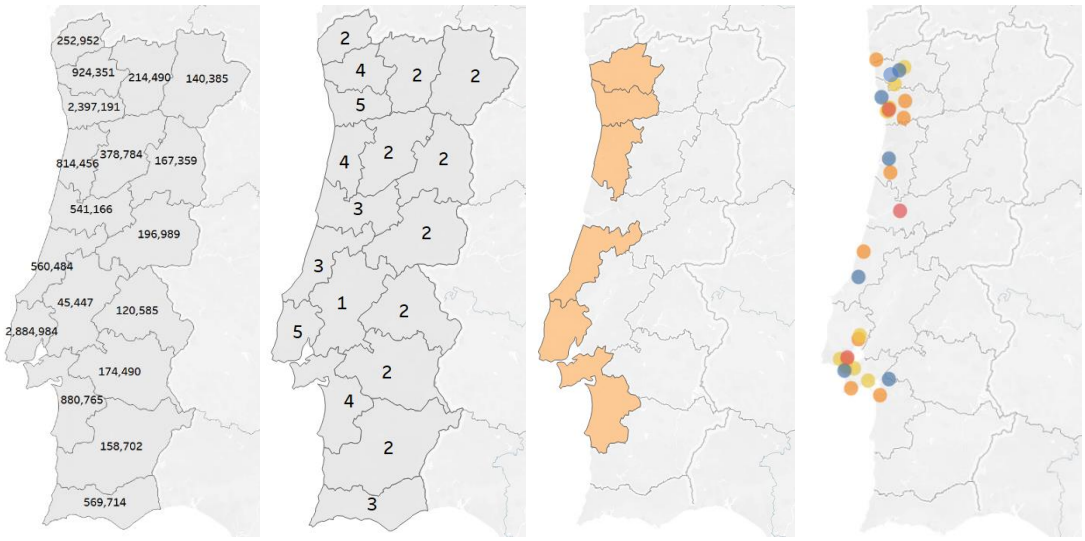

Figure 11 – a) Population per municipality; b) Activity level per municipality; c) Chosen municipalities; d) Collection points

5.2.2 Groups of Donors

IPST does not have groups of donors strictly defined. However, the institution perceives whom the target is when locating mobile or temporary fixed CCs. The institution also knows the targets to donate blood at hospitals and BCs, which are always open during the year. For instance, locating a mobile CC near universities shows that the targets for blood donation awareness are students, staff, and teachers. To simulate these groups of donors, centroids were generated randomly in the same way candidate locations for mobile and temporary fixed CCs. Due to dimensioning issues, the number of groups of donors generated per municipality was limited depending on its activity level. For municipalities with an activity level of 3, three groups of donors are considered, and four groups of donors are considered for municipalities with an activity level of 4 and 5.

The choice of the targets for each blood collection facility depends on a coverage radius. Donors do not usually travel long distances on purpose to donate blood. That is the reason why mobile CCs are so essential and efficient. A donor does not usually travel several kilometres to donate. However, when a mobile CC is, for instance, near the university or the job location, donors are more likely to donate, since the travel distance is no longer an issue (Osorio et al., 2018).

To consider the situation of donors not being willing to travel long distances to donate blood, a different coverage radius was considered for each type of facility where blood withdrawals are performed. For hospitals and BCs, the coverage radius considered is 5 kilometres. This coverage radius is justified by hospitals and BCs being facilities with a fixed location, which are dispersed in limited number throughout the country. The assumed coverage radius for mobile and temporary fixed CCs is 30 kilometres since these facilities increase the awareness for blood donation.

Figure 12 illustrates the coverage radius for each collection point and the facilities to which each group of donors can be allocated to donate blood. Groups of donors (black bullets) per municipality are covered by different facilities, allowing the model to choose which allocation is preferred.

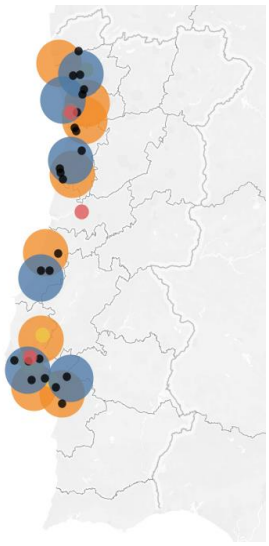

Figure 12 - Collection points coverage radius

5.2.3 Resources, Schedule, and Inventory Parameters

There are different types of facilities to donate blood hence different storage capacities are considered. Mobile CCs are considered to have a capacity of 300 blood pack units of WB collected from donors. For mobile CCs, the capacity is higher than in reality since, due to the previously mentioned dimensioning issues, the model does not support many candidate locations. As mobile CCs are considered to cover a higher range of groups of donors, a proportional capacity is ensured. The same reason justifies the upper bound for a daily distance of 300 km. Fixed CCs are considered to have a limit of blood collection of 200 blood pack units which is the capacity of the vehicle responsible for transporting blood from fixed CCs to BCs. For BCs, a capacity of 2000 blood pack units was set. Regarding BCs, a minimum inventory level of 50 blood pack units for RBC and 12 blood pack units for platelets was set. Additionally, the vehicles which transport blood from fixed CCs to BCs are the same vehicles responsible for transhipping blood pack units between BCs.

Mobile CCs are considered to have schedule constraints. They should leave from the respective BCs the earliest by 7 a.m. and arrive the latest by 11 p.m. During this service time, mobile CCs have a maximum length of time to be stopped in a location. Usually mobile CCs stay for a whole day in a location. However, blood potentials per hour are not constant. To overcome donors' arrival variability during the day, 4 hours of maximum length of holding time are defined for mobile CCs, as in the model, the blood potentials in one day per hour are constant. Regarding the time fixed CCs and BCs are available to perform blood withdrawals, the short number of hours considered is also due to the constant blood potentials per hour. Hence, the time fixed CCs and BCs are available to perform blood withdrawals is 2 hours. That is, donors' frequency in fixed CCs and BCs is lower than in mobile CCs. For hospitals and BCs, the available time is lower since these facilities have fixed locations, and donors do not usually travel long distances to donate blood. For the temporary fixed CCs, despite being located closer to the population than hospitals and BCs, the awareness among groups of donors is lower than mobile CCs. Table 5 summarizes the data for each resource, schedule, and inventory parameter.

Table 5 - Resources, Schedule, and Inventory Parameters

Resources Parameters	Data
Qm	300 un
Qv	200 un
Qb	2 000 un
$Dmax$	300 km
$Hmax$	4 hours
$OpenHf$	2 hours
$OpenHb$	2 hours

Schedule Parameters	Data
$departure$	7 a.m.
$arrival$	11 p.m.
Inventory Parameters	**Data**
$inil_{bpgt}$	RBC: 50 un Platelets: 12 un
$Imin_{bpg}$	RBC: 50 un Platelets: 12 un

5.2.4 Blood Products and Group Types

WB can be decomposed into four blood products: RBC, Platelets, Plasma and Cryoprecipitate. However, only RBC and platelets are considered in this study, as plasma and cryoprecipitate have the most extended shelf-life of 36 months. The shelf-life of RBC is 42 days, whereas, for platelets, it is considered 6 days, since, when stored at room temperature (+20ºC to +24ºC), the conditions are prosperous to bacterial organisms growth. Hence, in this case, the expiry date is up to 5 days only. However, if tests for bacterial detention are performed, platelets' shelf-life can be extended to 7 days. Thus, the way to consider both scenarios is by taking an average of 6 days. Before blood product production, WB donations are tested for several types of infection to ensure that the blood is disease-free. The tested samples are wasted, so a 0.02 minimum wastage factor was set. Additionally, RBC and platelets have a production factor of 1 and 0.25, respectively. One blood pack unit of WB collected from donors results in an RBC pack unit and a quarter of a platelet pack unit.

Regarding blood group types, this study uses the most common, namely the ABO and RhD systems. In this way, eight blood group types are considered in the model as well as the associated compatibility between group types shown in Table 2 (section 2.1).

5.2.5 Blood Potentials

All healthy and adult population should be considered as blood potentials for the entire country. In Portugal, 54 per cent of the population is between the age of 18 and 65, which is the eligible age for blood donation, however, in 2019, only 5.3 per cent of this eligible population was registered as a blood donor, and only 2.9 per cent donated (IPST, 2017b).

The data regarding blood potentials used is available at IPST's annual report of the Portuguese hemovigilance system corresponding to 2019. Apart from data regarding the number of donors registered, the number of donations, and the number of donors who have donated, the report presents the total number of donations per BC and hospital prepared to perform blood withdrawals. However, information on a municipality level is not available.

As mentioned in subsection 5.2.1, municipalities are the dimension chosen to deal with instances closer to reality. To calculate the blood potentials data for each municipality, the first step was considering the activity level. As

municipalities have different activity levels, the total blood potentials should not be distributed equally for the municipalities belonging to the respective BC. Instead, a weighted average was made with the activity levels, resulting in different and more realistic blood potential values for each municipality. Although blood potentials collected by BC have to be distributed per municipality considering a weighted average, blood potentials collected by hospitals were considered to be collected by the respective municipality. In subsection 5.2.2, it is mentioned that each municipality can have more than one group of donors. Thus, the total blood potentials of each district are equally divided among the groups of donors.

The proposed model considers the blood collected to depend on the number of hours a mobile CC, a fixed CC or a BC is open multiplied by the blood potentials per hour. Each municipality's annual blood potentials are deducted for daily blood potentials and then per hour of availability to perform blood withdrawals. As explained in subsection 5.2.3, the full-time mobile and fixed CCs and BCs are open is different. That is, the maximum availability time of mobile CCs are higher than for fixed CCs and BCs. With this, the blood potentials are considered per hour of availability time of mobile CCs. As fixed CCs and BCs have less visibility than mobile CCs, the consideration mentioned is another opportunity to penalize the choice of groups of donors donating blood at these facilities.

After defining blood potentials per hour and per group of donors, blood potentials are further divided per blood group types. Blood group type distribution in the Portuguese population varies according to Table 6 (Duran et al., 2007).

Table 6 - Blood group type distribution in Portugal

Blood group type, g	Distribution
AB+	2.9%
AB-	0.5%
B+	6.6%
B-	1.1%
A+	40.0%
A-	6.6%
O+	36.3%
O-	6.0%

Once this study is based on only one year of consumption, it is difficult to estimate from this sample which distribution is best suited to the blood potentials. Thus, the blood supply is modelled with a Normal distribution with mean μ, which is the estimation of groups of donors' blood potentials per hour times the probability of each blood group type explained above. The standard deviation is of five blood pack units. If the value resulting from the distribution is less than 0, then the blood potentials per hour are assumed to be 0. Therefore, blood potentials parameter is in blood potential per blood group type per hour.

5.2.6 Blood Demand

With the data presented in IPST's annual report of the Portuguese hemovigilance system for 2019, daily demand for each blood group type in each BC was estimated. The data available in the report refers to the annual

transfusion data per region. Thus, the annual demand per region was first transformed into daily demand placed at the respective BC. The demand per BC considers all the municipalities belonging to the respective decentralized national centre, however, since the number of municipalities to test in the model is restricted, the demand must be considered only for those. The distribution of the population per municipality was estimated by considering the population percentage of the municipalities chosen in the respective region's overall population. Finally, the daily demand is considered only for the percentage of the chosen municipalities' population. Blood group types were also considered in blood products demand.

Based on Haijema et al. (2007) and Duan & Liao (2014), blood demand can be modelled with a Poisson distribution. Therefore, to test the proposed model blood demand was assumed to follow a Poisson distribution with parameter l. This parameter is the estimation of the daily blood product demand per blood group type for each BC explained previously.

5.2.7 Costs

Cost information was not possible to obtain from IPST since they do not formally quantify most of the costs the model minimizes. Thus, literature was used to estimate all costs except for the opening temporary fixed CCs cost. Literature was not found for this perceived cost. The cost of transporting blood pack units between collections points, collection points and BCs, and between BCs is set to 0.14€/km based on values for refrigerated biological transport available in Rupprecht & Nagarajan (2015). According to Dillon et al. (2017) and Gunpinar & Centeno (2016), wastage and shortage costs for all blood products are set as 130€/unit and 1340€/unit, respectively. The substitution cost is calculated with the priority level for each blood group type and the shortage cost. The most preferred substitute has a cost of 1/8 of the shortage cost while the less preferred substitute has a cost of 7/8 of the shortage cost.

$$\nabla_{g'g} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1/8 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 2/8 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 3/8 & 1/8 & 1/8 & 0 & 0 & 0 & 0 & 0 \\ 4/8 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 5/8 & 2/8 & 0 & 0 & 1/8 & 0 & 0 & 0 \\ 6/8 & 0 & 2/8 & 0 & 2/8 & 0 & 0 & 0 \\ 7/8 & 3/8 & 3/8 & 1/8 & 3/8 & 1/8 & 1/8 & 0 \end{bmatrix}$$

When there is a shortage in one BC and oversupply in other, there is the opportunity to tranship blood pack units between BCs. This transhipment opportunity prevents a shortage event. Nevertheless, the transhipment cost simulates the lost opportunity of a BC with an oversupply of using the blood pack units to meet the demand at its DZs. Hence, transhipment cost is based on production costs established by the Portuguese decree-law 234-2015 and adding 200€ to the price per product to discourage this option strongly. Finally, opening a temporary fixed CC is assumed to incur in a setup cost, since opening a temporary location requires assembling the equipment and ensuring the proper conditions for blood donation to occur. This cost also works as a penalization for the low visibility for donors comparing to mobile CCs. Hence, it was assumed a perceived cost of 100€ for opening a temporary fixed CC.

As can be concluded, there are costs associated with more critical situations than others, particularly those which negatively and directly impact patients (shortage and substitution, for instance), followed by wastage as an unethical action and transhipment related to the non-self-sufficiency of BCs. Finally, the opening of temporary fixed CCs and the distance travelled does not impact patient service but represent costs for IPST. Although costs are already defined so that more critical situations are more costly, additional weights were created to control each cost term's importance. Wastage and shortage cost weigh 30 per cent, the former due to ethical concerns and the latter due to the potential risk of surgery cancellations or death. A 25 per cent weight is associated with substitution costs since this situation relates to bad quality patient service, according to Katsaliaki (2008). The last 15 per cent is equally divided for transportation, transhipment and opening temporary fixed CCs costs since these three indicators do not directly influence patients. Table 7 summarizes the data for each indicator cost parameter and its respective weight in the objective function.

Table 7 – Objective Function indicators' costs and respective weights parameters

Objective Function indicators costs	**Data**	**Indicators' weights**	**Data**
$transpC$	$0.14\ €/km$	θ	5 %
$wstC$	$130\ €/un$	θ'	30 %
$stgC$	$1340\ €/un$	θ''	30 %
$ABO\ substitution\ cost$	$\nabla_{g'g}.\ 1340\ €/un$	θ'''	25 %
$trspC_p$	$300\ €/RBC$ $400\ €/Platelets$	θ''''	5 %
$openfC$	$100\ €/f \in F^T$	θ'''''	5 %

5.3 Chapter Conclusions

In this chapter, the data collection and treatment procedures, as well as the assumptions and limitations considered, are described. Historical data from 2019 was used to estimate model parameters and generate daily and hourly data concerning blood demand and blood potentials. Blood potentials and demand parameters were assumed to follow a Normal and Poisson distribution, respectively. Due to lack of data, candidate locations for mobile and temporary fixed CCs were generated randomly. In addition, as the proposed model is complex, the test instance size had to be properly set. However, despite scenarios being small compared to reality, they are sufficient to prove that the proposed model contributes to the literature, since it can plan blood collections considering blood supply and demand uncertainty, blood perishability and blood group types substitution simultaneously. The following chapter describes the model application results for different scenarios.

Chapter 6: Results

In this chapter, the computational experiments' results based on the data described in the previous chapter are presented. The model was implemented in GAMS and solved through the IBM ILOG CPLEX solver version 12.8 in multi-thread mode. The experiments were conducted on a computer with two 6-Core 3.33 GHz Intel® Xeon® X5680 processors with 12 threads and 24.0 GB of RAM. In section 6.1, results are analysed, where the model was first run for two deterministic cases, and then the stochastic programming approach was run (section 6.2). Finally, section 6.3 presents the chapter conclusions.

6.1 Deterministic Cases

The model was first applied to a set of cases where blood potentials and demand parameters used are deterministic. The first case uses the input data presented in section 5.2, i.e. 2019 data, and is named Current Case (subsection 6.1.1). To understand how the proposed model reacts with a crisis, a Tragic Case is tested for two different weeks (subsection 6.1.2). The 2019 demand is considered to increase one hundred per cent in both weeks. However, in the first week, blood potentials are based in 2019 data while, in the second week, donations increase due to the increased awareness of the ongoing crisis.

6.1.1 Current Case

In this case, data unavailability is overcome by considering and treating annual data to build a scenario based on the Portuguese BSC case study. Despite not being a fully real representation, the scenario based on 2019 data is considered the Current Case. Testing the Current Case data in the model proposed provides an overview of the results in general. From these results, the general behaviour of IPST decisions regarding the blood collection planning is obtained, namely mobile CCs routes and the facilities location-allocation, i.e., the allocation of groups of donors to facilities where blood withdrawals are performed, which temporary fixed CCs to open, schedule definition for mobile and temporary fixed CCs and the quantity of blood to collect from donors. Furthermore, depending on the decisions, information of units' wastage and shortage are presented.

The Current Case considers an annual blood potential of 310 311 donations from 200 556 donors, from which can be concluded that each donor donates on average 1.55 times per year. Regarding blood demand, an annual demand of 284 187 RBC pack units and 27 138 platelets pack units is considered. Figure 13 shows the distribution of blood potentials and demand per region. Blood potentials in the North region are higher than in the Centre and Southern region. However, the blood demand is higher in the Southern region than in the remaining regions. Thus, as shown in Table 3 of subsection 2.6.2 and Figure 13, there is an unbalance between blood potentials and blood demand, particularly in CSTL. CSTL has the higher blood demand, but blood potentials are not equally high. The unbalance may indicate that there is a need for transhipment of blood products pack units between BCs.

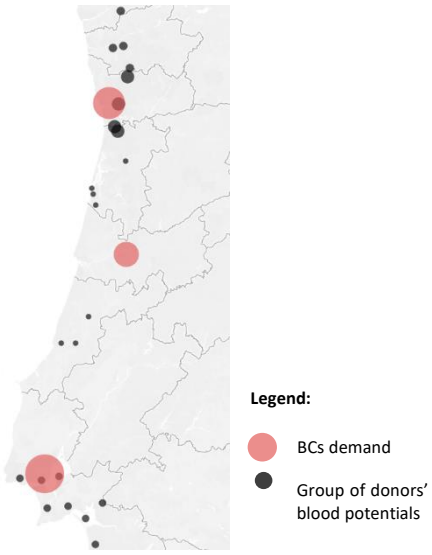

Figure 13 - 2019 blood potentials and demand distribution per region

The annual data of blood potentials and demand are converted into daily data. The blood potentials per hour are generated with a Normal distribution, while daily blood demand is generated with a Poisson distribution, as explained in subsection 5.2.5 and 5.2.6, respectively. The remaining parameters are constant among the scenarios. For a 7-day planning horizon, the parameters have resulted in a blood demand of 4 012 RBC pack units and 402 platelets pack units. The Current Case's general results are presented in Table 9.

Table 8 - Current Case general results

Collected Units	**Produced Units**		**Delivered Units**		**Transhipped Units**		**Shorted Units**		**Wasted Units**		
WB	RBC	Platelets	RBC	Platelets	RBC	Platelets	RBC	Platelets	WB	RBC	Platelets
4484	4394	1099	4012	402	526	5	0	0	90	0	184

The produced units indicator considers each blood product's production factor and the wastage factor for WB related to the sample used for the disease-free testing. The indicator results show that, for instance, considering the production factor of 1 for RBC units, the difference between the collected blood units and the RBC produced units is the result of the wasted unit's indicator for WB.

Regarding the delivered units, the indicator refers to the RBC and platelets pack units delivered by BCs to meet demand at the DZs. The delivered units' indicator results are the exact amount necessary to meet demand at the planning horizon, considering that there is no shortage of units. The absence of shortage relates with enough blood donations from donors as the produced units' indicator shows. Although there is 8.7 per cent of the RBC pack units not used to satisfy the demand in the planning horizon, 12 per cent of the RBC pack units produced are transhipped between BCs. These percentages mean that, at some time periods, there are BCs with not enough blood products to satisfy the demand. Therefore, there is a need for transhipment of blood products pack units from a BC with an excess of blood to others in need. Ideally, the transhipment flow should be zero, which means that each region should be self-sufficient. However, as previously mentioned, there is an unbalance between blood units collected and transfused. To encourage the BCs self-sufficiency, and as mentioned in the

previous chapter, there is a cost for transhipping units to discourage this option. Thus, the results presented for the transhipping unit's indicator are the lowest possible value aiming to satisfy the demand.

Finally, the wasted units' indicator refers to two types of wastage: the WB sample disposal used for the disease-free testing and the wastage of blood products units due to outdatedness. This indicator, as well as the shorted units' indicator, is one of the critical indicators to validate the planning effectiveness. Regarding the zero RBC units of wastage, the result is explained for this blood product since the planning horizon does not encompass the RBC shelf-life. For platelets, the wasted units' indicator results are explained by the high production factor comparing with the platelets demand. When blood is collected, its entirety must be processed, producing all the blood products and, thus, not having the opportunity to produce just the products in need. Although RBC demand is met during the planning horizon with lower wastage levels, as platelets demand is not proportionately high, platelets pack units are wasted. This wastage also results from the short shelf-life of platelets which do not allow to allocate the product with as much flexibility.

Another aspect that should be analysed is the need for blood substitution and transhipment per BC. The blood substitution indicator refers to blood products units of one blood group type, which are used to satisfy the demand of a compatible blood group type. The transhipment units' indicator, as previously explained, relates with lack of blood units in one BC which is filled by the transhipment of blood units from others with an excess. Table 10 indicates the results of both indicators per BC.

Table 9 - Blood substitution and transhipment per BC

BC	Substituted blood units		Transhipment units		
	RBC	Platelets	From	RBC	Platelets
CSTL	37	0	CSTC	297	2
			CSTP	203	0
CSTC	0	0	CSTL	0	0
			CSTP	0	0
CSTP	0	0	CSTL	0	1
			CSTC	25	2

These results allow us to verify that the Southern region's blood potentials are insufficient to satisfy the demand. Although there is transhipment from other BCs to CSTL, the transhipment is not enough. The RBC demand for a blood group type is satisfied with a compatible blood group type. However, this substitution is considered poor quality of service. However, as a shortage is worst regarding patient service, blood substitution is preferred. Moreover, the blood substitution indicator is zero for the remaining BCs.

An interesting aspect to observe is what blood group types are missing in the BCs. Figure 14 details the blood products demand and the blood products produced during the planning horizon.

As was expected, the overall blood demand at CSTL is higher than the blood produced. However, this unbalance is verified only for both blood group types with the highest population distribution, according to Table 6. More specifically, the transhipment from CSTC and CSTP to CSTL is mostly of RBC pack units of the A+ and O+ group types. CSTP also receives a transhipment from CSTC of RBC pack units despite in the overall planning horizon the blood produced being higher than demand. This transhipment results from a specific daily shortage in the BC.

Regarding platelets, the demand is lower than the amount produced due to the high production factor compared to the demand, as explained before.

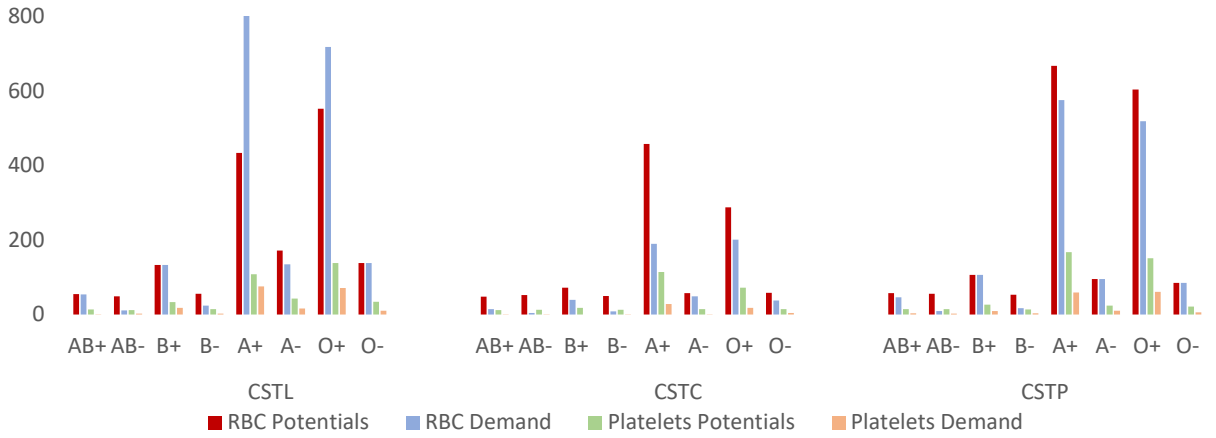

Figure 14 - Blood products demand and blood products produced per blood group type

The planning decisions to be defined by the model are the mobile CCs routes, group of donors allocation to each facility, the decision to open a temporary fixed CC, and the schedule for mobile and temporary fixed CCs to be available to receive donations. As the Current Case is analysed with a deterministic approach, the planning decisions are based on the blood potentials per hour in each day and the daily blood demand. The daily planning decisions obtained are represented in Figure 15.

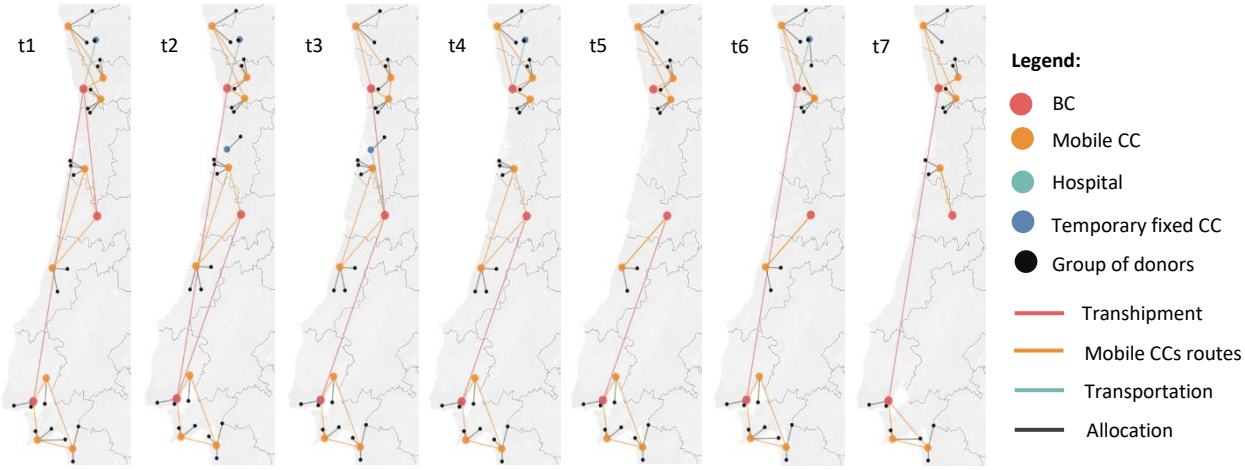

Figure 15 – Planning decisions

As shown in Figure 15, groups of donors are predominantly allocated to the nearest collection point. This allocation is in line with the lack of donors' willingness to travel long distances to donate blood. Moreover, the Southern region is the second region with the highest blood collection out of the three regions. Nevertheless, CSTL is the BC with the highest blood requests to satisfy the demand at Southern region DZs. Looking again at Figure 15, the unbalance between blood and demand at CSTL is addressed by transhipping blood products pack

units between the other BCs with an excess of blood to CSTL. For each time period, the unbalance is verified, and transhipment makes sure that there is no shortage of units at CSTL.

Regarding mobile CCs, Figure 15 shows that in the Northern region, the locations are visited during the 7 days. These visits are necessary since other BCs, such as CSTL, do not have more blood potentials to collect, and blood potentials from the North must be used to meet the demand of this BC in need. For the Centre region, the two respective candidate locations for mobile CCs are visited during the first four days. In the last three days, the CSTC demand can be met only by visiting one location. In the time period t5, blood collected from one collection of CSTC is enough to satisfy the CSTC demand in that day and to transhipment blood to CSTL to help meet the respective demand. For the Southern region, all the locations are visited by mobile CCs during the 7 days except in time period t7 in which a group of donors is not willing to donate, i.e., blood potentials of the respective group of donors are zero or very low, or the blood potentials already planned to be collected enough to meet blood demand and, therefore, the mobile CC does not visit the location. However, as the demand is higher than the blood potentials available, there is a need to request blood products from other BC.

Considering the temporary fixed CCs, in Braga's municipality, a temporary fixed CC is open in time period t1, t2, t4 and t6, when the group of donors in the coverage area is willing to donate coupled with the need to collect blood to meet demand. Also, in time period t6, one more group of donors is allocated to the temporary fixed CC since mobile CC's candidate location is not visited. This choice of donating in the temporary fixed CC only when there is no mobile CC nearby validates the significant awareness of mobile CCs and the donors' unwillingness to travel long distances. Therefore, donors choose first the nearest location. In the district of Aveiro, the temporary fixed CC opens only in time periods t2 and t3. Regarding hospitals and BCs, there is only one hospital and one BC in Lisbon, which covers a group of donors each. These two groups of donors donate during the whole planning horizon at the hospital in Lisbon and the CSTL.

The total cost for the Current Case is 201 982.18 €. This cost addresses direct and perceived costs for IPST, which are necessary to ensure a higher quality patient service. The highest indicator cost is the transhipment of blood units, representing 78.73 per cent of the total cost followed by the blood wastage and blood substitution with 17.62 per cent and 3.07 per cent. Distances costs are negligible in comparison.

Now that Current Case results are analysed, other scenarios can be assessed comparing to the Current Case. In the next section, a sensitivity analysis is performed considering the Current Case.

6.1.1.1 Sensitivity Analysis for Current Case

Given the inherent uncertainty of blood supply and demand parameters, a sensitivity analysis was performed. Blood potentials and blood demand are the only parameters that will be varied due to their uncertain nature. Therefore, a variation of ± 10 per cent is introduced in the 2019 blood demand. Regarding blood potentials, the variation of the 2019 donations is not linear. Considering that the number of donors which effectively donated is lower than the number of people registered as donors, the former is denoted as the usual donors. In addition, the usual donors are considered to donate throughout the year 1.55 times on average. Although usual donors only donate 1.55 times per year, male donors could donate up to four times a year and female donors up to

three times a year (SNS, 2016). With this information, fifteen scenarios were created. For each of the three demand scenarios, five blood potentials variations were considered: half of the usual donors donating one time, usual donors donating only one time, usual donors donating 1.55 times (which is the 2019 scenario), the registered donors donating 1.55 times, and usual donors donating three times, the last one to encompass the maximum donations per female donor. The variations are in ascending order of available blood potentials. With this, fifteen scenarios resulted from the variations of the uncertain parameters as Figure 16 depicts.

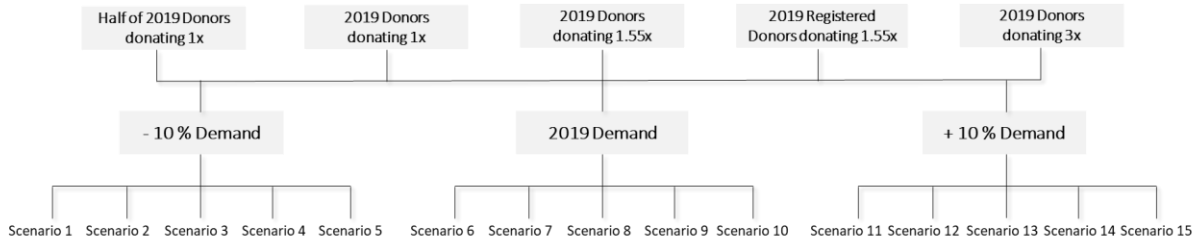

Figure 16 - Scenarios identification

After testing the fifteen scenarios, the graphs presented in Figure 17 and 18 summarize the total costs per scenario and the costs per objective function indicator per scenario.

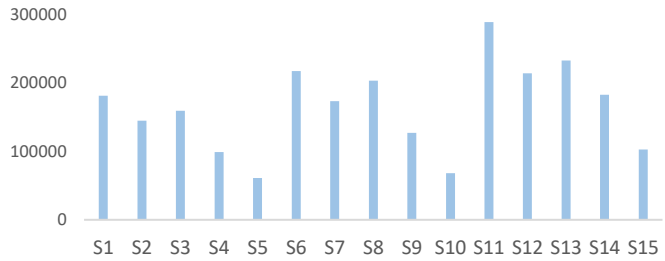

Figure 17 – Total Cost per scenario

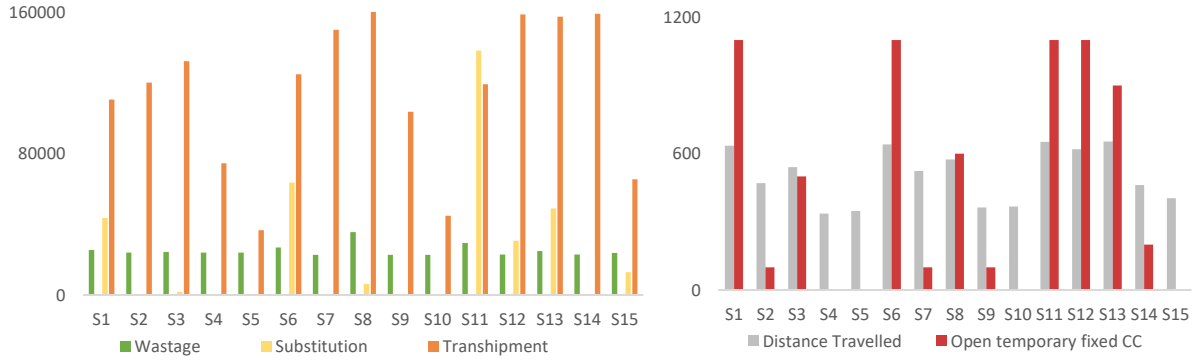

Figure 18 – Evolution of costs per scenario per objective function indicator

The first and most important thing to note with Figure 18 is that total costs vary considerably per scenario. Therefore, the solutions are very different. This variation let us conclude that not considering the uncertainty of blood supply and demand may lead to solutions away from reality. In section 6.5, solutions are analysed, which have resulted from testing the Current Case in the model with a two-stage stochastic programming approach.

Moreover, looking to the total cost between scenarios S2 and S3, S7 and S8 and S12 and S13, the total cost was expected to be lower due to the increase of blood potentials. Nonetheless, it is essential to remember that the blood potentials data were generated considering a normal distribution. Therefore, when blood potentials are referred to have increased because donors are considered to donate 1.55 times per year, the normal distribution mean increases. However, the distribution values vary following the normal distribution. That is, if a group of donors is willing to donate in a certain period in scenario S2, it does not mean that the same group of donors will be willing to donate in the same certain period in scenario S3 when the overall blood potentials of the year have increased. This consideration is valid also for the blood potentials of each blood group type. The number of donors with a specific blood group type is not linearly higher as the annual blood potentials. Regarding scenarios S2 and S3, S7 and S8 and S12 and S13, the blood potentials distribution throughout the country is less favourable considering the blood demand for each BC. Therefore, the solution to avoid shortage is to open temporary fixed CCs at locations where mobile CCs does not visit. The shortage is also avoided by transhipping blood between BCs and by using compatible blood group types to satisfy the demand if necessary. In this case, the distribution of blood potentials throughout the Northern and Southern region has decreased while the Centre region's blood potentials increase. This is another reason to enforce the need to consider the blood supply and demand uncertainty.

Regarding scenarios S1, S6 and S11, the costs are logically high. The lower blood potentials force IPST to open more temporary fixed CCs to collect blood from groups of donors not covered by mobile CCs. Also, transhipment is necessary to fill the shortage in a given BC as well as the use of compatible blood group types to meet the demand of patients' blood group type to avoid the delay of surgeries or even deaths.

Looking into scenarios S4 and S9, where all the registered donors donate 1.55 times and demand is -10 per cent of 2019 demand, respectively, the results are satisfactory. Comparing each scenario considered (S4 and S9) with the previous ones (S3 and S8, respectively), the solutions are more advantageous for IPST and patient service. With the higher supply of blood from donors, less temporary fixed CCs are open, diminishing vehicles' distance in transporting blood between temporary fixed Ccs and BCs. Also, in this case, each region is more self-sufficient, which decreases the need for transhipments between BCs and the blood group types substitution.

Considering the scenarios with higher demand and usual and registered donors donating 1.55 times (S13 and S14), if the 2019 demand would increase, it will be necessary that IPST will raise awareness and ensure that all the registered donors donate during the year. Figure 19 details the planning decisions for the first three days of these two scenarios.

If in the Current Case, during the 7-day planning horizon, mobile CCs have visited candidate locations forty seven times, with a higher demand more blood must be collected. Therefore, mobile CCs visited locations 55 times in S13. Three additional temporary fixed CCs were opened compared to the Current Case. Also, with higher demand, more substitutions were performed.

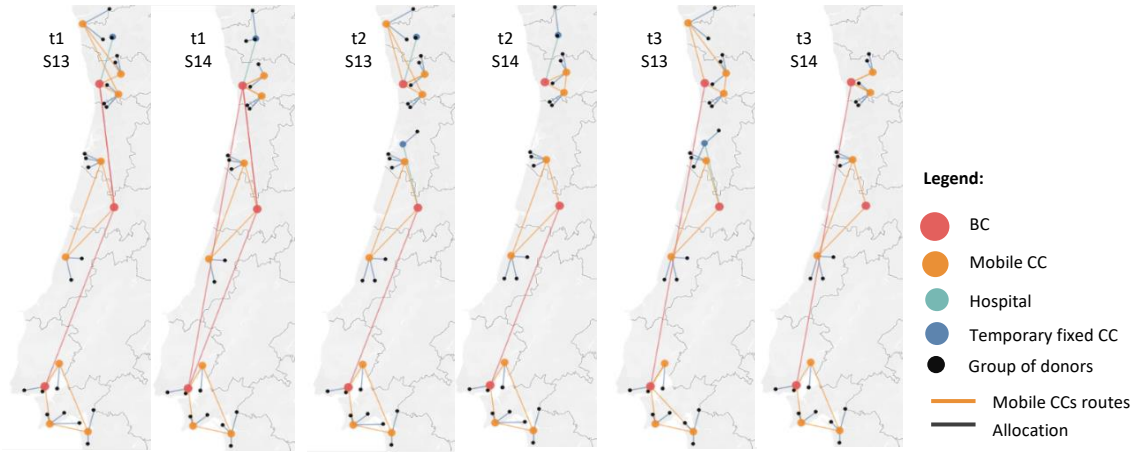

Figure 19 - Periods t1, t2, and t3 of Scenarios 13 and 14

However, with the higher awareness of all registered donors to donate blood to help patients in need, better results are obtained in response to IPST planning decisions. Looking at the Northern region of S14, the figure shows that mobile CCs cannot visit more than one location per period. As blood potentials have increased mobile CCs reached the maximum capacity only by collecting blood in one location. For instance, in time period t1 of scenario S14, as mobile CCs from CSTP are used to collect blood in Porto, Braga's temporary fixed CC must be opened to cover the groups of donors from the district.

Finally, considering the scenarios where usual donors donate three times per year (S5, S10, and S15), which is quite unusual but certainly possible, the results are significantly positives. The transhipment level reduces significantly, although these scenarios' optimal planning decisions do not turn CSTL into a self-sufficient BC. Regarding patient service, three donations per donor per year ensure a high level of quality service as blood substitutions are not necessary. Besides, IPST does not need to open temporary fixed CCs as BCs, hospitals, and mobile CCs cover enough groups of donors. With this, the necessary blood to meet blood products demand is collected.

To sum up, the results show that IPST's first step towards a better service level is to focus on higher visibility for donors. It is the way to engage them with the cause. In addition, this visibility can be improved by targeting more locations to be visited by mobile CCs to avoid the opening of temporary fixed CCs, which end up not being as efficient due to their lower awareness to donors.

6.1.2 Tragic Case

Blood is essential to survival. When a tragedy occurs, blood must be available in enough quantities to meet the unusual demand. Additionally, when a crisis occurs, blood demand is highly uncertain since patients are affected differently. Also, deaths occur if blood products are not available or blood potentials in the short term are not enough. Unfortunately, a country is hardly prepared with the right conditions when a crisis occurs (Abolghasemi et al., 2008). Therefore, planning decisions must be made to avoid shortages and guarantee patient service.

To understand how the proposed model reacts with a crisis, a tragic case is tested. This case is based on the 2019 annual demand, which is considered to increase one hundred per cent. Thus, for a 7-day planning horizon, the demand also increased. To assess the model behaviour, two weeks of the crisis are considered. In both weeks,

the demand is assumed to increase one hundred per cent. Regarding blood potentials, in the first week, 2019 blood potentials are considered. However, in the second week, donations increase (due to the increased awareness of the ongoing crisis) as if registered donors had donated 1.55 times during the year. This increase corresponds to 45 per cent more concerning 2019 donations. Table 11 summarises the general results per BC for the first week of the Tragic Case.

Table 10 - Tragic Case general results per BC

BCs	**Produced Units**		**Delivered Units**		**Transhipped Units**			**Shorted Units**		**Wasted Units**		
	RBC	Platelets	RBC	Platelets	From	RBC	Platelets	RBC	Platelets	WB	RBC	Platelets
CSTL	2273	568	2678	424	CSTC	408	35	1335	0	46	0	19
					CSTP	42	45					
CSTC	1590	397	1075	126	CSTL	0	2	80	0	32	0	49
					CSTP	0	0					
CSTP	2747	687	2647	264	CSTL	0	1	336	0	56	0	48
					CSTC	0	0					

As said before, a country is not always prepared for a crisis. Therefore, despite efforts, a shortage is expected to occur. Considering the information already presented regarding annual blood potentials per region, CSTL was expected to suffer the highest shortage levels. That is because the available blood potentials in the region are not proportional to the demand. In general, the shortage units represent 22 per cent of demand. This unbalance has a huge and negative impact on patient service.

Regarding transhipment units' indicator, compared to Table 9, the results show that CSTP has lower opportunity to tranship blood to CSTL than in the Current Case. Although the North region has the highest blood potentials level, an increase in demand forces CSTP to use the processed blood products units to satisfy their region demand. However, even with a shortage of RBC pack units, CSTP tranships units to CSTL. The reason for this transhipment is the overall goal of patient service provided by IPST. As IPST operates in the whole country, despite the preference for ensuring each region's self-sufficiency, the overall goal is the highest patient service in all regions.

Figure 20 illustrates the percentage per objective function indicators between Current Case and the first week of the Tragic Case. Looking at the comparison of both Current and the first week of a Tragic Case, many facts can be stated. Regarding distance travelled, the cost for the Tragic Case is slightly higher. Considering the costs of opening fixed CCs, with a higher demand the need to open fixed CCs has increased to collect blood from donors not covered by other facilities. Thus, the distance travelled increases as the collected blood units' transportation from fixed CCs to BCs happens more frequently.

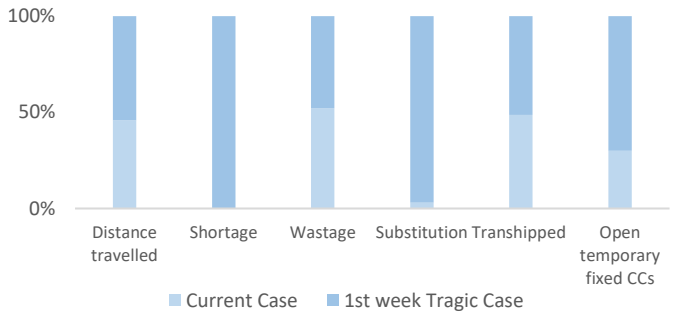

Figure 20 - Total cost comparison for the Current Case and the 1st week of the Tragic Case

As mentioned previously, the production factor of platelets comparing to the RBC production factor is high. However, since blood demand increased and considering the same blood potentials, more platelets pack units are used to meet demand reducing the blood products wastage. As the RBC production levels do not vary much between each case, the WB wastage level is identical. With this, the lower wastage cost of the Tragic Case is explained. Regarding substitution cost, in crises, all collected blood is vital. Although using compatible blood group types is poor quality of service, surgeries delays and deaths are worse. Thus, higher demand levels trigger a need to use compatible blood group types to meet the demand for another blood group type.

Finally, looking at the transhipment cost, for both cases, the cost is almost the same. However, the transhipment indicator has different behaviours for both cases. As mentioned previously, in the first week of the Tragic Case, CSTP has less capability to tranship blood to other BCs. The transhipment is mostly to CSTL as CSTP must meet region demand. Nonetheless, in the Current Case CSTP receive RBC pack units from CSTC while in the Tragic Case, the model opted to tranship the RBC pack units from CSTC only to CSTL. The model choice depicts the best solution to ensure the highest patient service in Portugal.

Assessed the first week of the Tragic Case, the second-week analysis of this case could help understand the differences in the planning decisions and the objective function indicators. Figure 21 illustrates the planning decisions for each week of the Tragic Case.

At first glance, Figure 21 shows that groups of donors visit all the possible locations where blood withdrawals can be performed during all two weeks, except one location in Lisbon on day 6 of the first week. These locations are the candidate locations for mobile CCs, fixed CCs, and BCs. The exception mentioned is related to the unwillingness to donate of donors' group, covered by the mobile CC that could have visited the candidate location. Even if the group of donors' blood potentials are low (but higher than zero), the model decided that it was not worth the visit of a mobile CC.

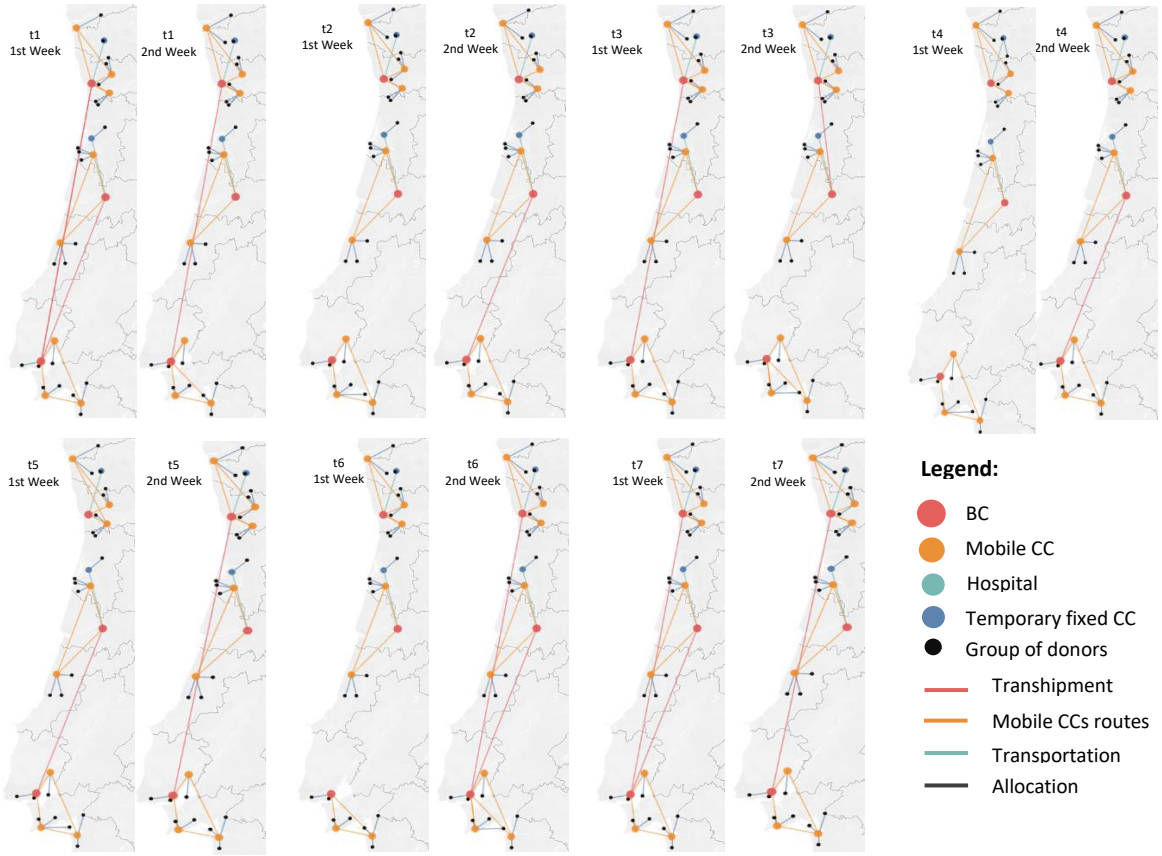

Figure 21 - Planning decisions for each week of tragedy

Another interesting thing to note is that during the first week on periods t2, t4, and t6, there is no transhipment between BCs. Being the first week of the crises, all the BCs are in shortage. Specifically, there is no opportunity for transhipment in these periods due to an excess shortage in all BCs. That is, the BCs that usually have excess blood to tranship for a BC in need have no opportunity to help other BCs since all of them are in shortage. Regarding the second week, in periods t1, t3, and t6 in the Southern region, the mobile CCs routes are shorter. As blood potentials are high, the mobile CCs capacity is not enough to collect blood from groups of donors just in one route. Thus, two mobile CCs are used to visit the locations in Lisboa and Setúbal.

The comparison between the total costs for two weeks during the simulated crisis is depicted in Figure 22.

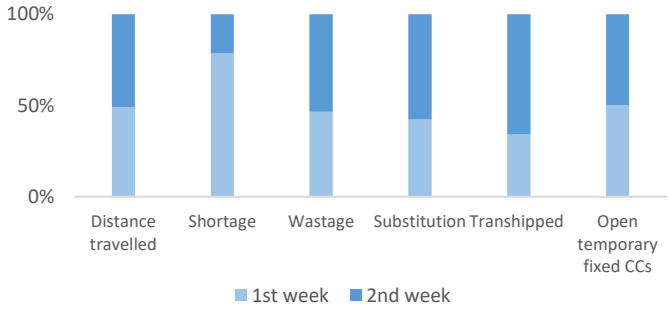

Figure 22 - Total Cost comparison for the two weeks of the Tragic Case

As expected, during the first week the total costs are higher than in the second week due to the higher shortage level. Since crises are not predictable, during the first week, blood donations are almost the same as during the

year, however, in the second week donors' awareness increases as well as the willingness to donate to help the population. This increase in blood donations has a significant impact on the shortage level.

In consequence of the donations increasing throughout the country, there is a higher opportunity to tranship blood from BCs with an excess of blood to BC in need. In addition, the higher availability of blood products of all blood group types allows the use of compatible blood group types to satisfy the demand of others which is better than death. Moreover, mobile CCs capacity becomes short in specific time periods which forces the use of more mobile CCs to visit the locations that in a typical day were visited only by one mobile CC. Thus, the distance travelled in the second week is higher than in the first week.

The Tragic Case analysis allows to state that the model proposed in this work is an efficient tool to simulate a crisis. With the simulation, conclusions can be made on which planning decisions to make, and capacity constraints should be changed. For instance, the number of hours facilities must be available for blood donations may be longer to collect blood from donors who may be willing to donate at different times from those planned for donations. With this, more mobile CCs must be used to collect blood in the same region. In this way, shortage levels may be lower.

6.2 Two-stage Stochastic Programming Approach

As stated before, blood supply and demand are uncertain parameters that may result in delays of surgeries or even death when mismatched. Therefore, as proved in section 6.1.1.1 with costs variability demonstration in Figures 17 and 18, uncertainty must be considered when modelling the BSC to obtain reliable planning solutions. Therefore, a two-stage stochastic programming approach was applied to the model.

The two-stage stochastic programming approach is based on scenarios to address parameter uncertainty. The scenarios must be defined previously, differing in blood demand and blood potentials levels, as well as their probability of occurring. While fifteen scenarios were defined to perform the sensitivity analysis for the Current Case, due to dimensioning issues, nine of these scenarios are used to test the model with the two-stage stochastic programming approach. These nine scenarios are those which usual donors donate per year only one time or 1.55 times, and registered donors donate 1.55 while the demand varies $\pm$10 per cent. These scenarios are chosen over the remaining scenarios where only half of the 2019 donors donate, or donors donate four times while blood demand varies $\pm$10 per cent. With these scenarios having a blood potentials level less similar than what currently occurs, the other scenarios were chosen due to similarity, and therefore more likeliness to occur, compared to the 2019 scenario. Figure 23 identifies the scenarios used.

To consider the probability of the scenarios, assumptions were made. Regarding blood demand scenarios probability, a -10 per cent variation is considered to have 10 per cent of probability to occur. Thirty per cent of probability was considered for the variation of +10 per cent of demand, leaving 60 per cent of probability for the 2019 blood demand scenario. The positive variation is higher than the negative because Portugal follows the worldwide trend in having an increasingly ageing population that requires more health care. Hence, the blood demand may increase due to the presence of chronic diseases and comorbidities in society.

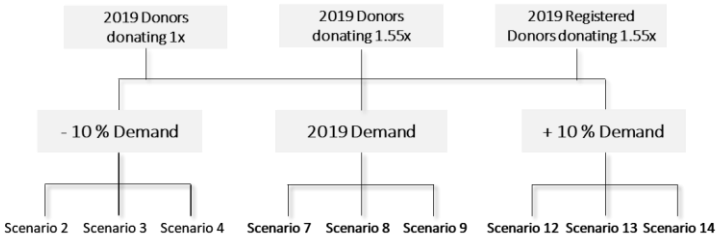

Figure 23 - Scenarios used for the two-stage stochastic programming approach

Regarding blood potentials scenarios, the scenario of usual donors donating 1.55 times per year is considered to have 65 per cent of probability while the scenario of usual donors donating one time per year is considered to have only 15 per cent of probability. Finally, all registered donors donating 1.55 times per year scenario has a probability of 20 per cent. The latter has a higher probability than the scenario of usual donors donating one time since nowadays the information is readily available, allowing IPST to reach a wider range of people. Table 12 summarizes the probability of each scenario.

Table 11 - Scenario probabilities

Scenario, s	Probability (ps)
S2	1.5%
S3	6.5%
S4	2%
S7	9%
S8	39%
S9	12%
S12	4.5%
S13	19.5%
S14	6%

With this, it is now possible to assess the performance of the proposed two-stage stochastic programming approach. After 30 hours, the solution was obtained with a gap of 6 per cent from the optimal solution.

Planning decisions for a 7-day planning horizon based on the scenarios detailed above are presented in Figure 24. Regardless of the scenario, mobile CCs routes, the location-allocation facilities, and which temporary fixed CCs to open are decisions taken earlier, for instance, at the beginning of the week.

One thing to note with Figure 24 is that during the 7-day planning horizon, all candidate locations for mobile CCs are visited. These visits per region are made only by one mobile CC owned by the respective BC, except in time period t1 in Southern region and in time period t2 in the Northern region where two mobile CCs are used to visit the respective locations. As mentioned in the previous sections, blood potentials are not uniformly distributed throughout the country for different scenarios. For this reason, allied with the differences of blood potentials availability and blood demand per scenario, the visit of all candidate locations may lead to inefficiencies for some scenarios or specific time periods. These inefficiencies are due to the visit of locations. However, groups of donors may not be willing to donate, or there is no need to donate blood as demand is balanced with the blood potentials already collected. In the case of BCs having enough blood collected to meet the demand, mobile CCs may choose

not to visit the location if this information is known in advance. However, as the schedule is published on the IPST website previously, mobile CCs must not fail with the appointment. The decision to not visit a location with the possibility of donors being willing to donate is bad quality of donors' service. In the proposed model, mobile CCs follows the schedule defined in the first stage, even if blood withdrawals are not performed by choice. However, in the real situation, blood is collected to avoid the lost opportunity of collecting one blood pack unit to meet unexpected demand.

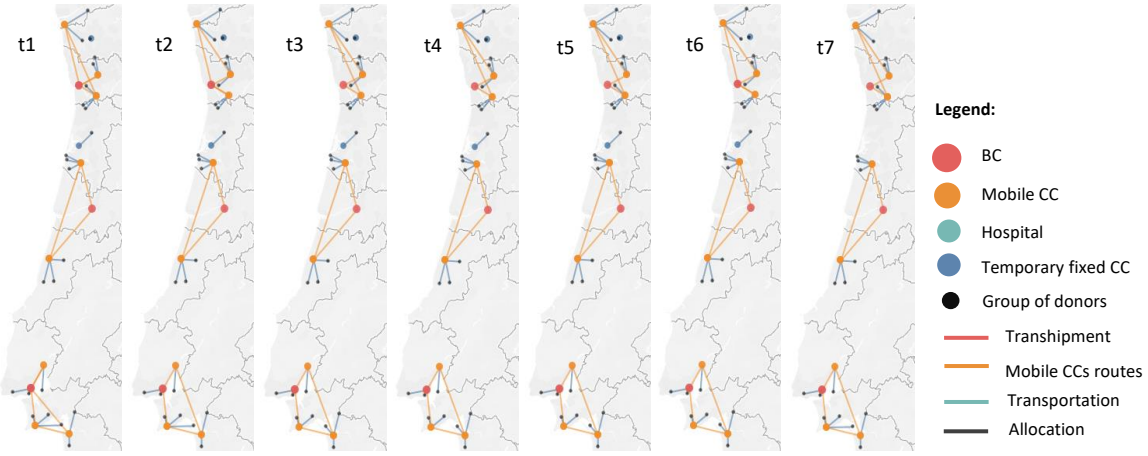

Figure 24 - Planning decisions when applying the two-stage stochastic programming approach

Figure 25 shows the number of mobile CC visits throughout the country during the 7-day planning horizon when applying the two-stage approach. Also, the number of visits is compared with the number of visits with blood collection as well as the number of visits per scenario when applying the deterministic approach.

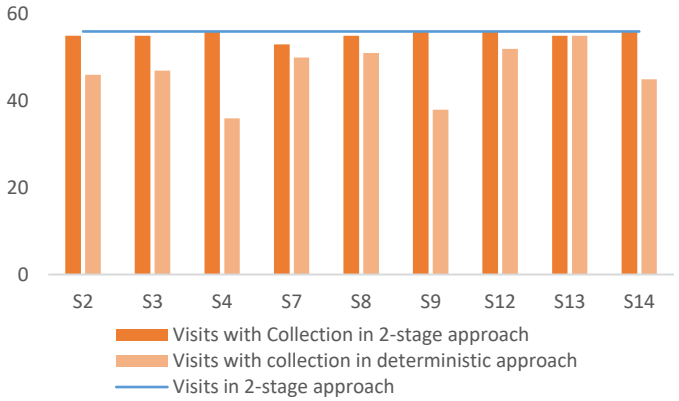

Figure 25 – Mobile CCs visits with collection per scenario per approach vs Mobile CCs visits in two-stage programming approach

Regarding the two-stage approach, only in scenarios S4, S9, S12, and S14 mobile CCs collect blood in all visited locations during the seven days of the planning horizon. Comparing the number of mobile CCs visits per scenario per approach, it is observed that the number of visits in the deterministic approach is lower, except in scenario S13, than when applying the two-stage stochastic programming approach. As mobile CCs schedule is already defined to visit all the locations, blood can be collected at any location as long as blood demand is satisfied at the lowest cost. Therefore, while in the deterministic scenarios there is opportunity to collect blood efficiently,

i.e., at the lowest cost possible and spending the least resources possible, in the two-stage approach this efficiency is not achieved, so the blood necessary to meet demand is collected at a larger number of different locations. However, it is essential to note that the stochastic programming approach returns a more robust solution since it regards nine different scenarios. The deterministic scenario returns a solution as if decision-makers have perfect information regarding parameters' events. As the latter situation is not realistic, the two-stage solution is more valuable since the solution has redundancy as it must account for the occurrence of the different scenarios considered.

Another thing to note with the blood collection planning depicted in Figure 24 is that, during the first six days of the planning horizon, temporary fixed CCs are open at the two locations that cover groups of donors (Braga and Aveiro). In the seventh day, no temporary fixed CCs are open. Although temporary fixed CCs are open, blood withdrawals may not be performed due to the groups of donors allocated to the respective temporary fixed CCs not being willing to donate blood depending on the distribution associated with blood potentials parameter, or there is no need to donate blood as demand is balanced with the blood potentials already collected.

Figure 26 depicts the number of times temporary fixed CCs are open during the 7-day planning horizon and number of times those perform blood withdrawals per scenario.

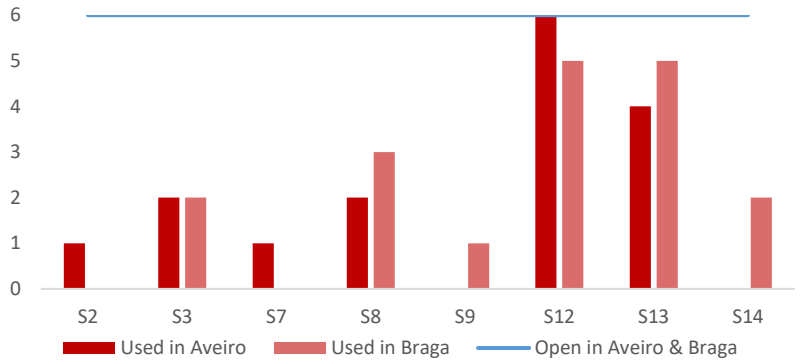

Figure 26 - Open temporary fixed CCs per location vs temporary fixed CCs used per location per scenario

As mentioned previously, the model recommends, for the 7-day planning horizon and all scenarios, to open the temporary fixed CCs in the first six days at Aveiro and Braga. From a prevention perspective for occasions with high demand compared to the available blood potentials, IPST ensures available facilities at all times. Considering the instance used, only in scenario S12, the temporary fixed CC opening rate at Aveiro is equal to its utilization rate. This unbalance creates inefficiencies in the blood collections planning. However, the most valuable performance indicator is patient service. Therefore, to ensure the facilities availability in case donors are willing to donate is preferable than a shortage in BCs and consequently, cause surgeries delay or even deaths.

It is interesting to assess planning decisions recommended by the model as well as their impacts on costs in the realization of each scenario. Figures 27 and 28 represent the total costs per scenario per approach and the costs per objective function indicator per scenario per approach, respectively.

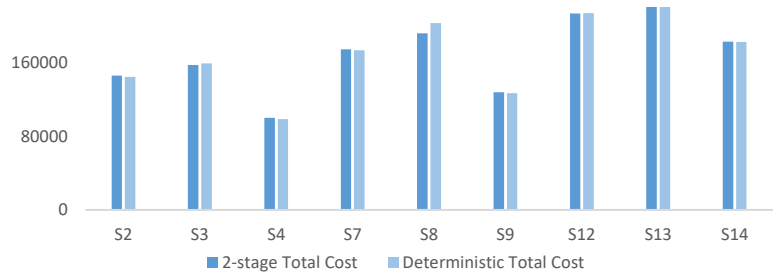

Figure 27 - Total Cost per scenario per approach

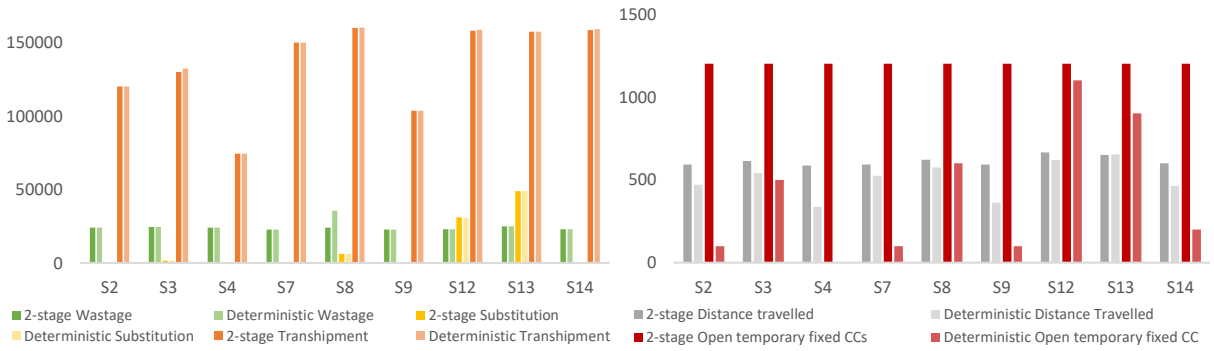

Figure 28 - Objective Function indicators costs per scenario per approach

In Figure 27, it is possible to observe that the total costs per scenario per approach are equivalent. That is due to the equivalence of blood wastage, substitution and transhipment costs which have much higher costs than the distance travelled and open temporary fixed CCs indicators even that these indicators have variations as observed in Figure 28. Fortunately, all the decisions ensure that shortage events do not occur whatever the scenario considered.

The objective function component “Distance travelled” represents the distance travelled by mobile CCs when visiting the locations to collect blood, and the distance travelled by vehicles that transport blood from fixed CCs to BCs. Regarding the two-stage approach, there is a variation of the distance travelled related to the distance travelled by vehicles since the transportation of blood units depends on the scenarios. Although temporary fixed CCs are open during the first six days of the planning horizon, there are time periods in different scenarios that blood withdrawals are not performed in these facilities. That is why the distance travelled indicator's variation is not always the same since there is no blood to transport from temporary fixed CCs to BCs every time temporary fixed CCs are open.

Despite blood collection planning being different between the deterministic and two-stage stochastic programming approach, the second stage costs are equivalent per scenario. That is due to the opportunity of facilities to choose how much blood to collect to meet demand. Even if there are more mobile CCs visits during the planning horizon, the blood collected per region is equivalent between approaches. Consequently, the blood wastage, substitution, and transhipment as the blood potentials distribution throughout the country is equal. However, and as explained previously, the two-stage approach's application may lead to inefficiencies for IPST since perfect information regarding uncertain parameters is not possible to obtain. Despite all candidate

locations for mobile CCs being visited and temporary fixed CCs are open for six days, it does not mean that blood withdrawals are performed. Blood withdrawals may not be performed due to the groups of donors allocated to the respective temporary fixed CCs not being willing to donate, or if there is no need to collect blood as demand is balanced with the blood potentials already collected. Inefficiencies are also considered when mobile or temporary fixed CCs only collect a small amount of blood pack units. Despite being inefficiencies when compared to having perfect information of uncertain parameters' events, it is not possible to state that the two-stage solution is worse than deterministic. Perfect information regarding uncertain parameters is not realistic. Therefore, the two-stage solution is a more robust solution having redundancy as it ensures high quality of patient service for the occurrence of the nine different scenarios considered.

Therefore, an inefficiency cost should be considered in the model to address these situations where IPST is spending resources in locations where donors are unwilling to donate. Suppose it is possible not to follow the schedule defined and published on the IPST website. In that case, a lost opportunity cost should be considered to address the situation where blood demand is already satisfied, and there is no need to visit a location. In other words, a lost opportunity cost for when blood potentials at the location whose visit has been cancelled could be used to meet the unexpected demand and avoid a shortage or a transhipment cost. This situation of not following the schedule previously defined also affects the quality of donor service.

6.3 Chapter Conclusion

After the presentation of the model implementation and validation, experimental results were assessed. Results analysis start with the assessment of deterministic scenarios and end with the analysis of the two-stage stochastic programming approach results.

First, a Current Case based on the 2019 data available at the IPST annual report is tested in the model. With the blood potentials and demand distribution considered, blood demand levels are higher in the Southern region, followed by the Northern region and the Centre. However, the Northern region's blood potentials are the highest, followed by the Southern region and the Centre. Despite the Centre region having the lowest blood demand and blood potentials levels, the latter is significantly higher than the former. With this, the transhipment between CSTC and the other BCs is frequent. Also, as the Southern region is the less self-sufficient, blood group types substitution occurs only at CSTL.

When comparing the Current Case with variations of itself, essential conclusions are taken through a sensitivity analysis. Fifteen scenarios were tested where the demand suffers a variation of ± 10 per cent, and five different levels of blood donations are considered. Regarding blood transhipment between BCs, the level only decreases when donors are considered to donate three times a year which is quite unlikely but possible. The distance travelled by mobile CCs and vehicles to transport blood between fixed CCs and BCs does not vary much per scenario. However, the number of temporary fixed CCs to open varies according to the blood potentials variation and not so much due to the blood demand variation. In addition, and as excepted, in scenarios with low blood potentials levels or low blood potentials and positive variation of demand levels, the blood group types substitutions increase.

The last deterministic case assessed is a Tragic Case where the Current Case demand is increased by 100 per cent in the first week. In the second week, blood potentials levels also increase. The planning decisions between the two does not vary much. However, with the parameters variation, the results of the indicators are very different. Between the first and the second week of the crisis, shortage level decreases much, as expected. This shortage decrease is achieved with increased transhipments between BCs due to the higher blood potentials availability. The higher blood potentials level also allows more blood group types substitutions which are preferable than blood shortage.

Finally, the two-stage stochastic programming approach is tested with the nine most likely to occur of the fifteen scenarios created for the sensitivity analysis. It is possible to conclude that the proposed solution is an effective solution approach to deal with uncertain parameters. In some scenarios, the model's planning decisions end up creating inefficiencies regarding the opening of temporary fixed CCs, location visits by mobile CCs and their respective utilization rate as if perfect information on the uncertain parameters' events were known in advance. However, as this situation is not realistic, the two-stage solution is a more robust and valuable solution when dealing with blood collections planning since it returns a solution ensuring a high quality of patient service for nine different and most likely to occur scenarios. Nevertheless, regarding temporary fixed CCs opening, there is 30 per cent of inefficiency while regarding the second the inefficiency is of 1 per cent as if perfect information was obtained. With this, it is concluded that an inefficiency cost regarding utilization rate should be considered. To underline, more important is to ensure a high quality of patient service no matter the scenario considered.

Chapter 7: Final Conclusions and Future Work

The BSC is a highly complex system designed to ultimately save lives. When extracted from the human body, the blood becomes a perishable product used for medical treatments such as surgery, organ transplantation, and cancer treatments. The unavailability of blood can cause deaths and complications for patients. Therefore, BSC is a system that improves population health outcomes. To do so, BSC systems operate multiple mobile CCs to collect blood from donors. It is the best way to create awareness for donors for blood donation. However, fixed CCs are also used to collect blood. These facilities where blood withdrawals are performed interact with BCs where blood is processed, the requests arrive, and blood products are distributed to different DZs.

In this dissertation, the Portuguese BSC, which is managed by IPST, is studied. The IPST has evolved since 1958 and nowadays collects more than 300 000 blood pack units per year from more than 200 000 registered donors. IPST's primary duties include deploying several mobile CCs to visit different locations throughout Portugal to collect from donors. To complement mobile CCs, temporary fixed CCs are open in locations near the population with the same goal of mobile CCs: to reach more donors to collect blood. The blood collected at hospitals and even at BCs is insufficient to meet blood demand during the year. That is because donors are not willing to travel long distances to donate blood. Therefore, mobile CCs and temporary fixed CCs are essential for balancing blood supply and blood demand. However, the deployment and opening of mobile and temporary fixed CCs, respectively, are not linear during the year. As a perishable product, blood must be collected and transfused within an interval corresponding to the blood product's shelf-life. Despite having to manage such a challenging system, IPST decision-makers rely on experience and practices to make complex planning decisions. Some of these decisions are the mobile CCs routes and their location-allocation, which are tactical decisions. Despite the importance of these decisions to guarantee blood availability to perform transfusions to patients, IPST does not have a tool to help in the decision-making, which addresses blood supply and demand uncertainty.

This research aims to use Operations Research techniques to improve the Portuguese BSC assisting IPST on blood collection planning to meet the uncertain demand and minimize wastage. Additional goals include (1) characterizing the Portuguese BSC; (2) understanding BSC functioning, highlighting its complex nature; (3) reviewing previous research on BSC planning, focusing on planning blood collections; (4) determining how to deal with uncertain environments and consider perishability and finally, (5) contributing to the literature by modelling, formulating and implementing an optimization model in a context based on the Portuguese BSC.

A literature review of planning decisions in the BSC context was performed, organized around uncertainty modelling approaches, products perishability consideration, and decisions regarding blood collections planning to attain these goals. It is concluded that this problem has been thoroughly studied under multiple approaches, from simple to very complex models that capture different aspects of BSC systems. Despite the research's richness, many approaches focus only on a particular BSC echelon or challenge or limit the blood collection planning to one to three decisions.

Exploring the insights of the literature review and the Portuguese BSC characteristics, a MILP model is developed. The model aims to minimize blood products wastage and shortage as well as the total costs associated with blood

collection activity while maintaining the service level and considering the characteristics of the BSC. To do so, mobile CC routes and the locations to visit to collect blood from the allocated groups of donors must be determined, as well as which temporary fixed CCs to open. Also, mobile and temporary fixed CCs schedule to perform blood withdrawals and the blood quantity to collect from groups of donors have to be decided. The model considers the opportunity to substitute a blood group type for a compatible one and blood products perishability. Most important, supply and demand uncertainty is addressed by applying a two-stage stochastic solution approach. Furthermore, an objective function is considered to provide the best possible service to donors and patients aligned with the lowest costs to achieve an optimized system, minimize costs associated with distance travelled by mobile CCs and vehicles which transport blood from fixed CCs to BCs; shortage, wastage; transhipment of blood pack units; substitutability of blood group types; temporary fixed CCs to open. To handle the objective components, different weights are considered to simulate the most critical objectives: those influencing the patient service, and the less critical, which influence ethical issues and IPST efficiency.

To apply the model to the Portuguese BSC, annual historical data from 2019 is considered. Due to dimensioning issues and lack of data, the instance size is appropriately set. However, it is enough to prove that the model effectively addresses all the decisions and characteristics regarding the BSC. Also, the planning horizon considered is seven days. Despite not being a realistic case-study, the proposed model is general enough to apply in different BSC from other countries. The data collection and treatment procedures necessary to transform annual data into model inputs are described.

To understand the model behaviour, several cases are studied. Before applying the two-stage approach, deterministic cases are analysed. The first case, called Current Case, is based on 2019 available data regarding annual blood collections and blood demand. To transform annual data into daily and hourly data, assumptions are made. Also, to consider some uncertainty even in a deterministic scenario, blood potentials and blood demand parameters are generated with a Normal and Poisson distribution, respectively. The results show that the Southern region is the only region that is not self-sufficient at all. Twenty-three per cent of the blood delivered by IPST to meet the Southern region demand is transhipped from other BCs. This occurrence is in accordance with 2019 reality. Transhipment has a high perceived cost to discourage this decision. However, as blood units shortage is worse, the model recommends the transhipment and therefore, the total cost of this Current Case is relatively high. Besides, another indicator whose results increase the total cost of this scenario is the wastage indicator. Regarding platelets wastage, 17 per cent of the platelets pack units produced are wasted due to high production factor compared to the orders rates and the short shelf-life, which does not allow allocating the product with more flexibility. Also, but not with a significant impact on the total cost, 2 per cent of the blood pack units delivered is from a blood group type to meet the demand of a compatible one.

A sensitivity analysis of the Current Case is performed with fourteen scenarios. Current Case suffers a variation of $\pm$10 per cent on blood demand level and five different levels of blood donations are considered to create these scenarios. Regarding blood transhipment between BCs, the level only decreases when donors are considered to donate three times a year which is quite unlikely but possible. From the scenario of only half of the usual donors donating one time to the scenario of donors donating three times, per demand variation, during the planning

horizon the temporary fixed CCs vary from opening eleven times to no times. During the 7-days, mobile CCs have the opportunity to perform fifty-six visits. For the best scenario, which is a - 10 per cent of demand variation and blood donors donating three times a year, mobile CCs only perform 63 per cent of the total visits allowed. For the worst scenario, which is a variation of + 10 per cent of blood demand and only half of the usual donors donating one time per year, 98 per cent of the visits are performed. A total cost variation of 79 per cent between the worst and the best scenario is proof that not considering the uncertainty of blood supply and demand may lead to solutions away from reality.

Before testing the two-stage stochastic programming approach, two more deterministic cases are tested. A Tragic Case is divided into the first week of the crisis and the second week. In both weeks the demand suffers a variation of + 100 per cent. Regarding blood potentials, in the first week, the usual donors donate 1.55 times, and in the second week, donor awareness increases, and all the registered donors are considered to donate 1.55 times. In the first week, 20 per cent of the blood demand is not met, and 16 per cent of the blood delivered by BCs is from compatible blood group types. However, in the second week, shortage levels are improved as expected. The shortage level decreases to 6 per cent. Since blood donations have increased, blood substitution opportunities increase to 18 per cent, which is better than a shortage, as well as the transhipment level, which increased from 7 per cent to 13 per cent. Also, as donors are more willing to donate blood, more temporary fixed CCs are open to collect as much blood as possible.

Finally, the two-stage stochastic programming approach is tested with nine of the fifteen scenarios created for the sensitivity analysis, and a probability for each scenario was estimated. The model recommends the visit of all locations during the 7-days planning horizon as well as the opening of the two temporary fixed CCs for six days. There are scenarios where the solution creates inefficiencies as the opening rate of temporary fixed CCs and locations visits rate for mobile CCs is higher than the respective utilization rate as if perfect information on the uncertain parameters' events were known in advance. Perfect information regarding uncertain parameters in the BSC is not realistic. Therefore, the two-stage solution is more robust and valuable, i.e., has redundancy since it ensures high quality of patient service for the nine different and most likely to occur scenarios. Despite an increase of 17 per cent between deterministic and two-stage stochastic programming approaches regarding the costs of the distance travelled by mobile CCs and vehicles that transport blood from fixed CCs to BCs, the two-stage solution is more reliable and robust since it is effective for different scenarios.

To sum up, the model is flexible in the scenarios it allows to consider, clearly presenting to the decision-maker how the system can and should evolve to different degrees of flexibility. This research's main contributions are a BSC system model with multiple facilities for groups of donors donate blood and the integration of the main concerns and particularities for proper BSC management.

7.1 Limitations and Future work

Several assumptions were needed to estimate model parameters in light of time and data availability limitations. In particular, possible candidate locations for mobile and temporary fixed CCs were generated randomly. Regarding the travel time and distance when mobile CCs leave BCs to perform blood collection or when vehicles

transhipment blood products between BCs, Google Maps functionalities help calculate this information. Also, travel times and coverage possibilities were assumed to be independent of the vehicle and remain unchanged over the planning horizon as well as the capacities of each facility that perform blood withdrawals. Moreover, IPST does not strictly define groups of donors, but groups of donors were defined with centroids generated randomly to consider the allocation. Due to dimensioning issues, the instance used is small compared to the real Portuguese BSC. Despite being a small instance, model behaviour is wholly assessed. Finally, costs estimates are based on public information, and some of the costs are considered to be perceived costs to penalize the indicator. Based on these facts and future work, more comprehensive Portuguese BSC cases should be studied.

Further suggestions for future work can also be identified. Regarding the mathematical model, the deferral time consideration should be modelled. A location should not be visited for fifty-six days when blood is collected from donors that are likely to donate in that location. Therefore, for instance, mobile CCs could be considered to visit the same location for one week in a row, and then, the next visit should be after at least fifty-six days. Also, a decrease in donations probability should be considered when a mobile CC visits the same location in consecutive days. The Portuguese BSC does not operate shuttles to pick up the donated blood at mobile CCs. However, allowing mobile CCs to stay over in a location for the next day instead of travelling to BCs every day could reduce travelling costs. Looking at the literature reviewed, some models consider the return of mobile CCs every day to BCs and models that only operate shuttles to pick up the blood collected from mobile CCs. The latter only returns to the BC at the end of the planning horizon. It could be interesting to consider both situations: to allow mobile CCs to return to BCs at the end of the day or stay over in a location being visited by shuttles. This consideration has never been made according to literature. Additionally, once mobile and temporary fixed CCs need staff mobilization, the staff allocation should also be considered in the model as it costs IPST. Moreover, as there are different collection methods such as apheresis method and MCA, they should be considered alternative donation methods. In addition, as there is an opportunity to choose the quantity of blood to collect to avoid blood wastage when applying a two-stage approach an inefficiency cost should be considered in the model to address these situations where IPST is spending resources in locations where donors are not willing to donate. For the occasions of not following the schedule defined since blood demand is already satisfied and there is no need to visit a location, a lost opportunity cost should be considered for when blood potentials at the location whose visit has been cancelled could be used to meet the unexpected demand and avoid a shortage or a transhipment cost. Finally, as the model performance is relatively low due to its high complexity, which creates dimensioning issues, different solution approaches could be considered. For instance, decomposing the model and solving in it in more than one step or using metaheuristics could be sufficient to obtain good solutions for larger instances and, consequently, overcome the BSC's complexity and the dimensioning issues of the model.

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Appendix A: Computational Results

Table 12 - Computational Results Summary

Experiment		Instance Characteristics		Instance Size		Computational Time (s)	Objectives	
		Municipalities	Collection points	Variables	Constraints		Cost	Gap (%)
Current Case		6	29	15538	16459	7463	16796.258	1.33%
Sensitivity Analysis	S1	6	29	15654	16414	3150	24111.717	0.00%
	S2	6	29	15626	16386	1923	13242.516	0.19%
	S3	6	29	15520	16279	2747	14384.979	0.97%
	S4	6	29	15628	16388	18000	10941.917	8.85%
	S5	6	29	15874	16634	3738	9051.406	0.18%
	S6	6	29	15672	16594	2235	30299.845	0.00%
	S7	6	29	15644	16566	1433	14356.371	0.00%
	S9	6	29	15646	16568	1267	12026.554	0.00%
	S10	6	29	15892	16814	1966	9078.334	0.25%
	S11	6	29	15666	16538	3689	49380.241	0.67%
	S12	6	29	15586	16458	1804	60363.075	0.00%
	S13	6	29	15532	16403	956	27631.401	0.00%
	S14	6	29	15640	16512	1841	14829.644	0.25%
	S15	6	29	15886	16926	10800	13644.026	1.47%
Tragic Case	1st week	6	29	15674	16928	28801	765056.644	3.10%
	2nd week	6	29	15734	17256	28800	279979.861	0.00%
Two-stage stochastic programming approach		6	29	58710	104071	107137	17959.451	6.01%