TÉCNICO LISBOA

Development of models to optimize IPST blood collections

Joana Isabel Nunes Alves

Thesis to obtain the Master of Science Degree in

Information Systems and Computer Engineering

Supervisors: Prof. Pedro Tiago Gonçalves Monteiro
Prof. Maria Inês Camarate de Campos Lynce Faria

Examination Committee

Chairperson: Prof. José Luís Brinquete Borbinha
Supervisor: Prof. Pedro Tiago Gonçalves Monteiro
Member of the Committee: Prof. Daniel Rebelo dos Santos

October 2021

Acknowledgments

I would like to acknowledge professor Pedro Tiago Gonçalves Monteiro and professor Maria Inês Lynce Faria for accepting me in this adventure and believing in me, and for their unconditional support and remarkable orientation and dedication throughout the development of this thesis. All your availability and the support you have given me throughout this journey gave me confidence and motivation to carry out this work.

I would like to thank IPST and all the people involved in the LAIfeBlood project for their collaboration and for the data provided, without which it would not have been possible to develop this work. The database complies with current legislation for the protection of data, in this case, from benevolent blood donors - their identity being unknown. Data were used for academic purposes only.

I would like to thank my friends for the laughs and tears shared in these last years and the many more to come, for all the help they gave me, and for never doubting me. They were always there for me during the good and bad times in my life. They certainly helped me grow as a person and made these years a memorable experience. Particularly to Rita for all the hours shared on the train, all the study sessions and the exchanged notes, and all the memories we built together, thank you for always being there.

I would like to thank my family for all the support and encouragement throughout all these years. Especially to my parents for giving me this incredible opportunity and trying to understand and support me in the most difficult times. To my sister for always being there to listen to me and always having on the tip of her tongue the right words, and for making me laugh when I feel like crying. Without you and your unconditional support, this would have been an impossible journey.

I would like to thank the Fundação para a Ciência e a Tecnologia (FCT) for the national funds that supported this work within the project UIDB/50021/2020 and the project LAIfeBlood - Inteligência Artificial para a Gestão do Sangue, with reference DSAIPA/AI/0033/2019.

Abstract

The blood supply chain includes the activities of collecting, processing, inventorying, and distributing blood and its derived components from donors to patients. The ultimate goal of managing the blood supply chain lies with the challenge of balancing storage and wastage of blood units to ensure that blood is available when needed and at the same time guarantee that the number of wasted blood units is minimal. Blood donors play an indispensable role in the blood supply chain as they are the only current source of human blood. But blood donation is a voluntary and unpaid activity, so the supply of donor's blood is irregular. On the other hand, the demand for blood products is highly stochastic. Thus, it is necessary to motivate donors to donate blood to ensure there are no shortages.

The present work aims to characterize the Portuguese blood supply chain and propose an optimization model to deal with decisions concerned with blood collection planning, contributing to its improvement. To do so, an integer linear programming approach is developed, establishing the optimal locations for mobile blood collection facilities and the donors' allocation to the collection points with the goal of minimizing the total costs of the blood supply chain.

The Instituto Português do Sangue e da Transplantação, which is the entity responsible for managing the Portuguese blood supply chain, provided data on historical blood collection records that allowed us to recognize the needs and restrictions involved in the collection of blood, which enabled obtaining a more correct mathematical formulation. The developed model was validated with the provided data, allowing the consequent obtainment of the optimal locations for blood collection facilities.

Keywords: Blood Supply Chain, Blood Donation, Optimization, Integer Programming

Resumo

A cadeia de abastecimento de sangue inclui as atividades de colheita, processamento, inventário e distribuição de sangue e dos seus derivados, desde os dadores até aos pacientes. O objetivo final da gestão da cadeia de abastecimento de sangue reside no desafio de equilibrar o armazenamento e o desperdício de unidades de sangue de forma a garantir que o sangue está disponível quando é necessário e, ao mesmo tempo, garantir que o número de unidades de sangue desperdiçadas é mínimo. Os dadores de sangue desempenham um papel indispensável na cadeia de abastecimento de sangue, pois são a única fonte atual de sangue humano. Mas a doação de sangue é uma atividade voluntária e gratuita, pelo que as dádivas de sangue são irregulares. Por outro lado, a procura é altamente estocástica. Assim, é necessário motivar os dadores a doar sangue para garantir que não há escassez.

O presente trabalho pretende caracterizar a cadeia de abastecimento de sangue Portuguesa e propor um modelo de optimização para lidar com as decisões relativas ao planeamento das colheitas de sangue, contribuindo para a sua melhoria. Para isso, é desenvolvida uma abordagem de programação linear inteira, estabelecendo os locais ideais para as unidades móveis de colheita de sangue e a alocação dos doadores aos pontos de colheita, com o objetivo de minimizar os custos totais da cadeia de abastecimento do sangue.

O Instituto Português do Sangue e da Transplantação, que é a entidade responsável pela gestão da cadeia de abastecimento de sangue Portuguesa, forneceu dados com registos históricos das colheitas de sangue, que nos permitiram reconhecer as necessidades e as restrições envolvidas na colheita de sangue, permitindo-nos obter uma formulação matemática mais correta. O modelo desenvolvido foi validado com os dados fornecidos, permitindo a consequente obtenção dos locais ideais para os pontos de colheita de sangue.

Palavras-chave: Cadeia de absatecimento de sangue, Doação de sangue, Otimização, Programação Inteira

Contents

List of Tables

List of Figures

Acronyms

BSC Blood Supply Chain.

CST Centro de Sangue e Transplantação.

CSTC Centro de Sangue e Transplantação de Coimbra.

CSTL Centro de Sangue e Transplantação de Lisboa.

CSTP Centro de Sangue e Transplantação de Porto.

ILP Integer Linear Programming.

IPST Instituto Português do Sangue e Transplantação.

MILP Mixed Integer Linear Programming.

RBC Red Blood Cells.

SCM Supply Chain Management.

Chapter 1

Introduction

This chapter starts with the motivation for the development of the present work in section 1.1. Then, the proposed objectives are listed in section 1.2, along with the contributions, and finally, the structure of the document is described in section 1.3.

1.1 Motivation

Human blood is a scarce resource. It can only be produced by human beings and currently there are no other products or chemical processes that can be used to generate blood [1].

The importance of blood in our lives has been recognized since its discovery, even before it was realized that it was responsible for the transport, regulation, and protection of our bodies. In 1613, the English physician William Harvey discovered how the blood circulation mechanism works: the heart pumps blood to the body through the arteries, and the blood returns to the heart through the veins. This discovery allowed the development of the first experiments with blood transfusions. A blood transfusion is a process of administering blood or a blood component from one individual, the donor, to another, the recipient, through a tube inserted into a blood vessel. Transfusions are necessary in situations where there is a substantial loss of blood or a deterioration of the functions of one of the blood components, for example, in patients treated for blood disorders (severe anemia, cancer, leukemia, among others) or during or after surgery.

The blood supply chain (BSC) ensures that blood is available when needed, such as in emergency procedures, surgical operations, or routine medical treatments. As a result, an effective healthcare system should incorporate a well-thought-out plan for managing the BSC. Blood supplies are, in fact, a critical component of the healthcare infrastructure that helps save people's lives in everyday medical situations [2]. A principal characteristic of blood supplies is their perishable nature. By definition, a perishable product has a limited lifetime during which it can be used and after which it should be discarded [3]. Perishability of blood and blood components (red blood cells (RBC), platelets, white blood cells, and plasma) contributes to making even harder the management of the BSC. Given the BSC's complexity and associated costs, its ultimate goal is to provide safe and adequate blood supplies. The BSC includes the activities of collecting, processing and testing, inventorying and distributing blood and its components from donors to patients [4].

Managing the BSC comprises the challenge of balancing storage and wastage of blood units. Due to the perishable nature of blood products, storing an excessive number of blood units could result in outdates, which raises ethical issues as people voluntarily donate blood to help those in need, being its waste viewed with disapproval by society. On the other hand, having shortages may be tragic since lives can be lost if there is no available stock when it is needed, which consequently leads to an increase in the

mortality rate. Moreover, the nature of blood is unpredictable, as the supply of donor's blood is irregular and the demand for blood products is highly stochastic [5], making it a challenge to match supply and demand to avoid the wastage and shortage of blood products.

In addition to the characteristics mentioned above for each blood component, such as their different shelf-lives and very own purpose and use, there is another one contributing to increasing the complexity of managing the BSC. RBC are the main mediator in blood transfusions, making them one of the most important blood components, but there are specific rules regarding the compatibility of these products that must be followed during a blood transfusion so that it is safe for the patient. Since human lives are at risk, it is evident the importance of a good management of the blood supply chain.

Due to the irregularity of the blood donor's supply, blood is a product that is becoming increasingly limited. In fact, the number of blood donations has dropped, in general, to a new low. In Portugal, donation numbers have been decreasing in the last nine years [6]. So, blood donation must be encouraged in the population to reverse this drop in donation numbers. The management of blood donations is made at the collection stage, the first echelon of the BSC. At this stage, decisions about the optimal locations of blood collection facilities are made to ensure that the blood demands are fulfilled.

Thus, considering the importance of the product in question, particularly the fact that it can only be produced by human beings, as well as the challenges in the BSC that will be addressed in Chapter 2, blood collection management is a subject that deserves to be studied. Furthermore, the literature on the Portuguese BSC is scarce. In this context, the objective of this work is to develop a mathematical optimization model to deal with decisions concerned with the planning of blood collections and characterize the Portuguese BSC.

1.2 Thesis Objectives and Contributions

The present work is a collaboration with Instituto Português do Sangue e da Transplantação (IPST) with the goal of characterizing the Portuguese blood supply chain and proposing an optimization model for the planning of blood collections, contributing to its improvement. The main goal of the developed model is to minimize the total costs of the BSC while determining the optimal location for collection points in order to guarantee that all blood demand is satisfied. In this way, there is the need to analyze the Portuguese blood supply chain to understand how it works and what aspects are involved at each stage of the BSC. Furthermore, it is necessary to study what has been done in the healthcare area regarding the supply chain's management to understand the concepts involved in its management and be able to apply them to the Portuguese BSC.

The contributions offered by this work are twofold. First, there is not much literature focusing on the Portuguese BSC, in fact, there is only one article published in 2020 on this subject [7], and to the best of our knowledge, the collection echelon of the BSC was never studied in Portugal. Thus, this work aims to close this gap. Second, the main goal of this work is to contribute to the efficient management of the BSC. So, a generic mathematical programming model is presented to optimize the planning of the blood collections. An overview of state of the art is presented to explore the different methodologies that are applied to BSC issues, with a particular focus on the methods used in the collection echelon of the BSC. An optimization model based on integer programming is proposed to locate mobile blood collection facilities while the total BSC costs are minimized. For the development of the proposed model, data related to blood collection records were first analyzed so that the proposed model correctly describes the collection echelon of the BSC. Afterward, the developed model was validated with historical data from IPST, demonstrating a real-world application of the proposed model. Additionally, a more general mathematical formulation is presented, considering aspects of the BSC other than the collection echelon.

1.3 Thesis Outline

To make this document easier to read, it is essential to outline the structure adopted and summarize the main content of each chapter. All chapters begin with a brief introduction where the content of the chapter is discriminated and end with a summary on the subject discussed. Thus, this dissertation is structured as follows:

- **Chapter 1 - Introduction**: is the present chapter, where the thesis theme is introduced, contextualizing the problem under study, defining the objectives and contributions of this work, along with the document structure.
- **Chapter 2 - Background**: is presented Instituto Português do Sangue e Transplantação as responsible for managing the blood supply chain in Portugal. The main characteristics of the blood supply chain are described, including its functioning and the relationships between its various echelons. This chapter tries to present general views of this supply chain to facilitate the comprehension of the literature review that is carried out in the following chapter.
- **Chapter 3 - Literature Review**: a literature review is conducted identifying the current best practices regarding blood supply chain problems and decisions. This chapter aims to demonstrate how the management of blood supply chains has been addressed in the literature to decide which approach is indicated to represent the problem at hand.
- **Chapter 4 - ILP Formulation to Optimize Blood Collections**: the problem under study is described in more detail and the proposed mathematical formulation is presented. This chapter aims to develop a model that accurately represents the current functioning of blood collections in Portugal. An additional formulation is also provided, allowing the model to be more generic and applicable to different scenarios.
- **Chapter 5 - Experimental Evaluation**: the results of the application of the optimization model are presented. The aim of this chapter is to demonstrate the applicability of the developed model and carefully analyze and discuss the obtained results.
- **Chapter 6 - Conclusions and Future Work**: is the final chapter where the main points and the most relevant conclusions are summarized. Future work to be developed about this topic is also pointed up.

Chapter 2

Background

In this chapter, a brief description of the entity responsible for the regulation and management of the Portuguese blood supply chain, namely Instituto Português do Sangue e da Transplantação (IPST), is made. To better understand the main product of this work, a succinct description of the blood is presented, following the history and structure of IPST. Then a characterization of the Portuguese BSC is made with a summary of each of the echelons identified. Finally, to better model the Portuguese BSC, it is necessary to understand its needs and restrictions, so collection and transfusion trends on data gathered from IPST are analyzed.

2.1 Blood

From whole blood can be derived more than a hundred different products [8], but red blood cells (RBC), white blood cells, plasma, and platelets are the most important and most used components. Each blood product has its very own purpose and it is used in different situations. RBC are needed in anaemia treatments, while plasma is used to treat burns. Platelets are indicated for cancer patients [4].

RBC are the most prevalent cells in the blood and contain the protein hemoglobin, which transports oxygen to our cells. Plasma is a yellowish liquid component of whole blood that is derived by eliminating RBC. White blood cells are immune system cells that protect the body from infectious organisms. Platelets are clotting factors found in plasma that are involved in the coagulation process, which helps the body heal after a wound or bleeding [1]. As blood, its components are perishable products, and each one has its shelf lives. While plasma has a shelf life of a year, RBC can only last up to 42 days, and platelets are the most critical component with a shelf life of just 5 days [4]. Due to this characteristic, if a blood product has not been transfused before the end of its shelf life, it must be discarded.

When talking about blood, there is another feature that must be taken into consideration. In 1901, Karl Landsteiner discovered the "ABO" blood group. “ABO” blood types are polymorphic, antigenic, and genetic substances, which are established on RBC surfaces and some other cells and tissues [9]. "ABO" and "Rhesus" blood types are the major human blood type systems, being highly important in transfusion medicine [10]. Blood groups are characterized by small carbohydrate epitopes, which depend on the presence or absence of genes “A” and “B” positioned on the 9q34 chromosome. “ABO” blood type system comprises four major “ABO” phenotypes “A”, “B”, “O”, and “AB”. There are eight major blood types: A^+, A^-, B^+, B^-, AB^+, AB^-, O^+, and O^- [11]. Each blood group has a different distribution in the population that varies between ethnicities and geographical regions, which makes some blood types extremely rare. Although some blood types are rare, the truth is that only some of these blood groups are compatible with each other and can be substituted. The aim is to use every patient’s blood type as much

as possible [2], but when a patient's blood type is not available, it is possible to use another compatible blood type, existing specific restrictions and preferences in using different blood types once the use of a non-compatible blood type can have disastrous consequences for the patient. Nevertheless, blood substitution can help prevent shortages.

2.2 Instituto Português do Sangue e da Transplantação

2.2.1 History

In 1958, the first organic structure responsible for transfusion medicine was created, designated by Instituto Nacional do Sangue (INS) (National Blood Institute). Despite this first effort, a clear definition of the strategic policy was not achieved which contributed to an ineffective coordination. In the 80's, the shortage of blood and the emergence of new transmissible diseases, like AIDS, highlighted the absence of a clear and efficient national organization able to implement a precise definition of a set of rules to be applied from collection to transfusion of blood. Later, in 1990, it is created the Instituto Português do Sangue (IPS) which appears as a public institution with technical, administrative and financial autonomy, and which integrates the personalized services of the Health Ministry. In 2012, IPS is renamed to its current denomination, Instituto Português do Sangue e Transplantação (IPST), after being merged with transplantation services [12].

IPST ensures, at a national level, the activities of collection, processing, storage and distribution of human blood and its components, the national management of the Portuguese registry of bone marrow donors, the processing, storage, and distribution of human organs and tissues, and human derived cells, such as umbilical cells [6]. In collaboration with the relevant national and international authorities, IPST is also responsible for verifying the proper functioning of the National System of Hemovigilance and the National Biovigilance System. Both systems focus on collecting information on unexpected or unwelcome effects from donors, from the collection to the transfusion of blood and blood components, and take measures to prevent the occurrence or recurrence of some of these incidents/events [12].

IPST's vision is to continue to promote blood donation to contribute in time and quality to human life. In this sense, IPST promotes good practices and research in the fields of science and technology, mainly in the domains of transfusion medicine, transplantation, and regenerative medicine [12].

2.2.2 Structure

IPST is a central institution with jurisdiction over the entire national territory, with its headquarters in Lisbon. Its organs are the board of directors, the tax auditor and the advisory board of blood, histocompatibility and transplantation [12].

In 1994, the regional areas of activity of the regional blood centers of Lisboa, Porto and Coimbra were fixed, and their operational areas are mapped in figure 2.1:

- Centro de Sangue e Transplantação de Lisboa (CSTL) is responsible for the southern region - regions of Lisboa e Vale do Tejo, Alentejo and Algarve, respectively the yellow, green and dark blue areas of figure 2.1;
- Centro de Sangue e Transplantação de Porto (CSTP) covers the northern region, the light blue area of figure 2.1;
- Centro de Sangue e Transplantação de Coimbra (CSTC) is responsible for the center region, the orange area of figure 2.1.

Figure 2.1: Main Centers' area of activity.

These centers are referred to as the main blood centers in the developed model.

2.3 Characterization of the Portuguese Blood Supply Chain

The Portuguese blood supply chain is similar to Canada's blood supply chain [13] and Iran's blood supply chain presented by Zahiri et al. [14]. A simplified version of the Portuguese blood supply chain network is illustrated in figure 2.2. The first level represents the donors, the second the collection points that can be either mobile or fixed, then there are the main centers, and the last level represents the demand points. Donors can donate blood at either mobile or fixed collection facilities. The collected blood is then shipped from the collection points to the main centers, where the whole blood is analyzed and separated into different components. The blood components are stored at the main centers until they are needed by demand points.

The Portuguese BSC network is more complex than the one presented in figure 2.2. In reality, there are blood transportations between main centers and between the hospitals themselves. But in this

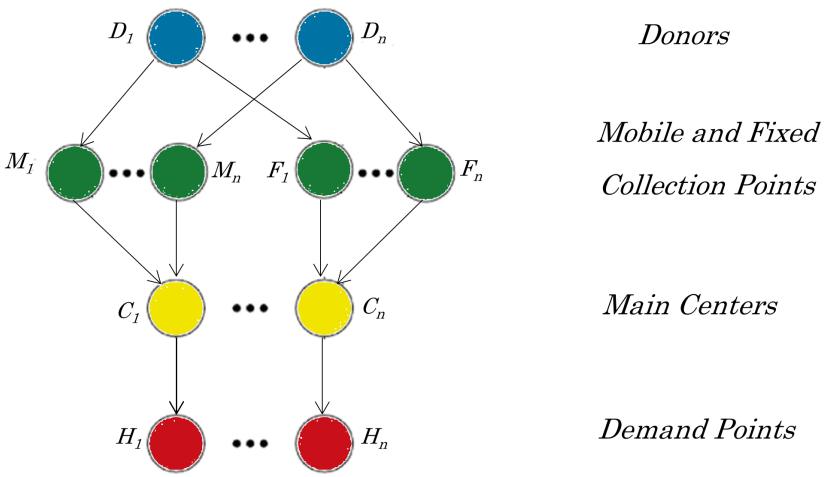


Figure 2.2: Blood supply chain network in Portugal (adapted from [7]).

modeling approach, we only consider the relations depicted in figure 2.2. And, despite being remarkably complex, Osorio et al. [4] concluded that the blood supply chain could be simplified considering only four echelons: Collection, Production, Inventory, and Distribution. The identified echelons are presented in figure 2.3 and will be addressed below.

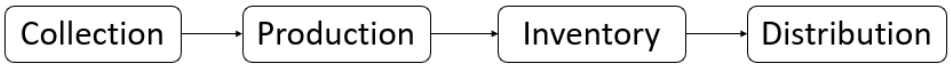


Figure 2.3: Echelons of the blood supply chain.

2.3.1 Collection

The Collection stage is the first echelon of the BSC and its purpose is to obtain the amount of blood and blood products needed to meet demand. This sufficient amount of blood products is achieved by promoting donation in the population. At this stage of the BSC decisions are made regarding location and capacity of collection points and which collection methods to use.

In Portugal, blood donations are anonymous, voluntary, and unpaid. To be able to donate blood, the donor must be healthy, weigh at least 50 kg and be between 18 and 65 years of age. Other more specific criteria like the family medical history, allergies, among others, are evaluated through a questionnaire carried out by the donor and a detailed clinical interview with a doctor before the donation. About the frequency of donation, there must be a minimum interval of 2 months between donations as long as it does not exceed 4 and 3 donations in a year, for men and women, respectively.

Voluntaries can donate blood at either mobile or fixed collection points, as previously mentioned. Fixed collection points are permanent all year and are usually located in hospitals, while mobile collection points are scheduled for a specific day at a certain location. This planning is done annually by the main centers and the donors associations, but tactical decisions, such as human resources allocation and equipment required, are done on a monthly basis.

Regarding collection methods, there are two main methodologies to be used [4]. The first method is the most common and consists in the collection of one unit of whole blood (approximately 450 ml, representing about 10% of the human blood) that it is later separated into its components in the Production stage. The second method is called aphaeresis and the donor's blood is passed through a machine to collect only the desired components (platelets, RBC or plasma) and then the unwanted components return to the donor [4]. This method allows for greater donation of each component, but requires a greater time commitment from the donor, which is the reason why this method represents a minority in the volume of donations, and consequently, will not be considered in the proposed model. The materials used to carry out the blood collection are the collection bags and tubes. The bag must be within the validity period and must be well labeled, including the collection date, expiry date of the collected blood unit, donor number, and collection number.

The collected whole blood and the blood components coming from apheresis are then shipped to main centers for testing and production of blood products.

2.3.2 Production

In the Production stage, the units of blood received at main centers are tested for known diseases and separated into its components. Whole blood must be kept inactive for two hours before processing and is viable for up to 24 hours after collection. Firstly, the blood samples from donors undergo a laboratory analysis, where eligibility tests are carried out, and the blood group of each sample is determined. If the

samples pass the test, i.e., the blood units are accepted and transfusable, the collected blood units follow to the fractionation phase. In this phase, the blood units are separated by centrifugation into their blood components. This separation process is dependent on the type of bag used in the collection stage. After this separation, blood products are preserved in an additive solution to ensure their viability and durability. Finally, each product is stored respecting its different storage conditions and shelf-life time. The bags containing the products are relabeled, respecting the previous information presented in the collection bag, by adding the fractionation information.

At this stage of the BSC, decisions include exploring fractionation alternatives and the advantages of collection methods to improve the overall performance of the BSC.

2.3.3 Inventory

During the Inventory stage, most of the decisions are related to the definition of inventory policies. Because of blood products' short shelf-life, inventory management of these products is particularly challenging. For good blood inventory management, a trade-off must exist between having a sufficient amount of blood products to supply any patient's need and avoid the wastage of those products. The main objective of this echelon of the BSC is to balance supply and demand so that the costs related to inventory management are minimized.

Inventory management is carried at both the main center and hospital levels, with a minimum inventory level defined based on the capacity to respond to an emergency.

2.3.4 Distribution

The Distribution stage is the last echelon of the BSC, but distribution decisions can be found along the entire supply chain since this stage occurs whenever there is movement of blood, either whole blood or other blood products. Distribution processes can be related to transporting blood from a main blood center to a hospital blood bank, from one main blood center to another (if there is a shortage in one location and oversupply in another), or from the hospital blood bank to their place of use.

Typically, hospitals make daily blood requests to the nearest main blood center, based on historical data, predictions and empirical clinical knowledge. This regular blood allocation is made in the morning, while urgent requests can be made during the day [4]. The distribution policy of blood units and its components depends on the main centers. However, there is a tendency to follow a FIFO (First In First Out) methodology that assigns first older units to demand points, due to the components' perishable nature.

2.4 Collection and Transfusion Trends

This section aims to demonstrate the panorama of collection and transfusion of blood and blood components in Portugal over the last few years. The data presented in the following sections were obtained from a report on the Portuguese hemovigilance system published in 2019 by IPST [6]. Every year IPST publishes a report analyzing the activity of the national blood transfusion network and establishing patterns and trends based on data from recent years, which is essential for a better understanding of the reality in Portugal. Through the publication of these reports, it is also possible to analyze and manage the risks associated with the collection and transfusion of blood in Portugal, along with outlining strategies to increase its safety and sustainability, through the implementation of preventive and corrective measures adapted to our reality.

2.4.1 Collection Trends

Table 2.1 shows collection data from 2011 to 2019, with donor and donation numbers, and some donation rates, at a national level. It is visible that over the past nine years, the tendency for a decrease in the number of donors and donations has maintained, with the annual rates being negative over time. However, in the last year, this negative trend of the donation rate per 1000 inhabitants and the donor index per 1000 inhabitants was less accentuated compared to 2018.

Table 2.1: Collection trends between 2011 and 2019.

	2011	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**
Number of donors	271 159	249 168	237 826	226 882	223 924	217 431	210 904	203 177	200 556
Donors / 1000 inhabitants	27,12	24,92	23,78	22,69	22,39	21,74	21,09	20,32	20,06
Variation of donors (%)	-8,26	-8,83	-4,79	-4,80	-1,33	-2,99	-3,09	-3,80	-1,31
Number of donations	410 889	391 331	361 819	353 459	337 580	334 022	324 053	314 091	310 311
Donations / 1000 inhabitants	41,09	39,13	36,18	35,35	33,76	33,40	32,41	31,41	31,03
Variation of donations (%)	-2,12	-5,01	-8,15	-2,35	-4,72	-1,07	-3,08	-3,17	-1,22

In order to better understand the regionalization of blood collection and its patterns, table 2.2 shows collection data from 2019 according to the geographic region. In 2019, IPST through blood collections in its three main centers, CSTP, CSTL, and CSTC, collected 57,24% of all collected blood at the national level. It can be seen that the CSTP is the center with the highest collection values of the three IPST centers, followed by the CSTL, and lastly, the CSTC. Moreover, comparing the Portugal regions' collection values, the Northern region, without considering donations made directly in the CSTP, is the one with the highest collection numbers, having collected 19,23% of the total collected blood, followed by the Southern region that represents 14,08% of the whole collected units, not including donations at the CSTL. The Central region, not considering the blood collected in the CSTC, is the one that has the lowest collection values, representing only 5,69% of the whole collected blood, without considering the islands' regions.

Table 2.2: Collection trends per region in 2019.

IPST/Region		**Collection**	**%**	**%**
IPST	CSTP	73 123	23,56	57,24
	CSTL	56 160	18,10	
	CSTC	48 338	15,58	
Northern		59 666	19,23	19,23
Central		17 612	5,69	5,69
Southern	Alentejo	12 311	3,97	14,08
	Algarve	10 036	3,23	
	Lisboa e Vale do Tejo	23 569	7,60	
Islands	Madeira	5 886	1,90	1,90
	Açores	3 537	0,96	0,96
Total		**310 311**		

2.4.2 Transfusion Trends

Table 2.3 shows the transfusion trends between the years 2014 and 2019 for RBC at a national level. By analyzing the table, it is visible a tendency for a decrease in the number of RBC transfusions over

Table 2.3: Transfusion trends for RBC between 2014 and 2019.

		2014	2015	2016	2017	2018	2019
RBC	Number of units	328 101	312 924	306 841	300 334	290 001	293 892
	Variation of units (%)	-3,11	-4,63	-1,94	-2,12	-3,44	1,34
	Number of patients	99 205	92 271	93 864	93 801	91 642	91 734
	Variation of patients (%)	-3,17	-6,99	1,73	-0,07	-2,30	0,10

the last years, which is demonstrated by the negative variation of both units and patients transfused. However, in 2019, there was an increase in both the number of RBC transfused units and transfused patients compared to 2018.

In table 2.4, there is the transfusion data for RBC in 2019 per country region. The Southern region (Alentejo, Algarve, and Lisboa e Vale do Tejo) accounts for 46,18% of all the national transfusions, being the region with the highest transfusion values. Considering that this region is not the one with the highest collection numbers, this value is very high, indicating that the other country regions need to contribute to satisfying the needs of the Southern region, meaning it is not self-sufficient. The Northern region performed 31,14% of all transfusions at the national level while the Central region is responsible for 19.38% of the transfusions.

Table 2.4: Transfusion trends per region in 2019.

Region	**Transfused RBC**	**%**
Alentejo	11 551	3,93
Algarve	10 724	3,65
Centro	56 968	19,38
Lisboa e Vale do Tejo	113 433	38,60
Norte	91 511	31,14
Madeira	5 336	1,82
Açores	4 369	1,49
Total	**293 892**	

Through the analysis of figure 2.4, it can be concluded that, over the last years, there was a decrease in the number of transfused RBC units that had been accompanied by a drop in the number of donations and donors. In 2019, there was a slight growth in the number of transfused RBC units, but this was not followed by an increase in the number of donations.

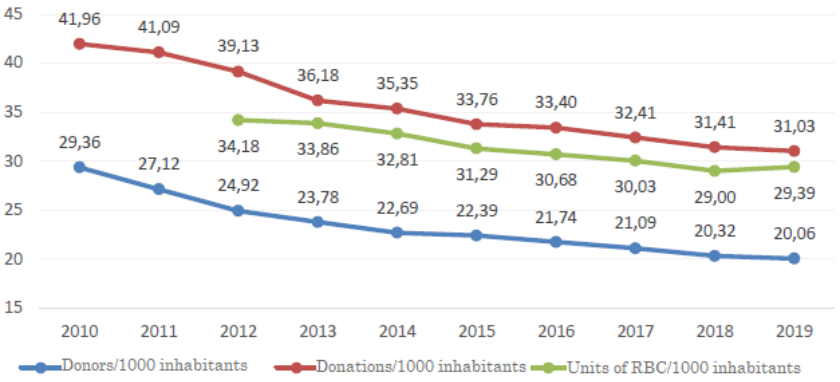


Figure 2.4: Comparison of donor, donation and RBC transfusion rates per 1000 inhabitants between 2010-2019.

By analyzing the historical data presented above, the Southern region is the one at the national level with higher needs for RBC, accounting for almost 50% of transfusions in 2019, but it is not the region with higher collection values. This region is served by the CSTL that has the second lowest collection numbers, being the CSTP the main center with the highest number of collected units. These facts show the importance of good blood supply chain management at a national level, with some regions being the ones that consume the most, although there are not the ones that collect the most, with the need to transport RBC from one region to another.

2.5 Summary

In this chapter, the institution in charge of managing the Portuguese blood supply chain, IPST, is presented. Then, the Portuguese blood supply chain is characterized, identifying four echelons: collection, production, inventory, and distribution. Finally, collection and transfusion trends show the panorama of collection and consumption in Portugal, emphasizing the need for good management of the blood supply chain.

In the following chapter is addressed what has been studied already about these topics.

Chapter 3

Literature Review

In this chapter, an outline of relevant literature on blood supply chains is provided. Firstly, to better understand the underlying concepts of the problem, a brief definition of supply chains and supply chain management is provided and is addressed their application to the healthcare area. Secondly, the literature review papers are analyzed. Finally, the studied literature from the earliest developed works to more recent models is organized according to the solution method used. Particularly, integer programming models are the main focus of this work.

3.1 Supply Chain and Supply Chain Management

According to Min and Zhou [15], the supply chain is composed of a series of synchronized processes to acquire raw materials and components, transform them into finished products, add value to the product, and, finally, distribute them. Throughout all the needed steps to deliver the product to the end customer, there is the interference of several entities that exchange information and resources between them [16]. This chain is commonly characterized by a forward flow of materials and a backward flow of information [17].

The processes that make up a supply chain can be differentiated into internal or external logistics processes. The first group includes processes related to materials management, including the acquisition, storage, production, and shipment of finished products. On the other hand, external logistics handles the distribution of the product to the end customer and includes activities such as receiving and processing orders, storing and handling inventory, outbound transport, and returns. Thus, Supply Chain Management (SCM) is defined as the integral and strategic coordination of the various functions of the entities that make up the supply chain, with the aim of improving the long-term performance of the individual entities and the supply chain as a whole [16].

In other words, SCM can be defined as the management of upstream and downstream relationships with suppliers and customers in order to deliver superior customer value at less cost to the supply chain as a whole, according to Christopher [18]. SCM involves the process of planning, implementing and controlling the operations of the supply chain in an efficient way [19]. Supply chain network design (SCND) is the most important strategic decision in SCM, playing an important role in the performance of the supply chain. In general, SCND includes determining the optimal locations, numbers, and capacities of the network facilities and the aggregated material flows among them [20].

The importance of adequate management of supply chains has been studied by several authors, especially in the context of the manufacturing industry (Flynn et al. [21], Cao and Zhang [22]). However, supply chains are found in every line of business and not just in a particular industry. SCM is an important

issue for many sectors such as energy [23–27], healthcare [28–33], and waste management [34–36].

3.1.1 Healthcare Supply Chain Management

SCM is the essence of healthcare delivery. Its quality is dependent on the availability of medical supplies at the right time and in the right quantities to the patients, a lack of which may generate customer dissatisfaction [37]. Mathur et al. [37], in 2018, presented a literature review on the relationship between supply chain practices and supply chain performance, having the premise that the higher the efficiency of the supply chain, the better the performance of the organization.

Albarune et al. [38] recognized the importance of the application of SCM to the healthcare sector, identifying and overcoming some of the challenges to its adoption. The authors proposed a model on valued supply chain management to be integrated into hospital management. Polater and Demirdogen [39] also studied this topic, revealing supply chain flexibility has a mediation effect between supply chain integration, demand forecasting, supplier performance, and patient responsiveness.

Applications of operational research in healthcare are reviewed by Papageorgiou [40] and Rais and Viana [41]. The issue of healthcare supply chain practices has been researched over the years to improve the performance of healthcare supply chains, allowing a more efficient response to the patients' needs. Rajagopalan et al. [33] presented a multi-period set covering model for determining the minimum number of ambulances and their location. The authors validated their approach through a simulation model. Zahiri el at. [42] developed a multi-period location–allocation model for the design of an organ transplant transportation network under uncertainty. The model aims to minimize the total cost as well as the total traveled time in the network. Araz et al. [30] proposed a multi-objective covering-based vehicle location model for emergency services. The proposed model goals are to maximize the population covered by vehicles, maximize the quantity of population with backup coverage, and increase the service level by minimizing the traveled total distance from selected locations to cover all zones.

Another crucial aspect of the healthcare supply chain is the perishable nature of its products. The challenge associated with these products concerns their deterioration over time, as they have a short period during which they can be consumed after being produced. At the end of this period, these products have to be discarded, ending not being consumed by anyone. This characteristic enforces the importance of planning every activity in the supply chain to reduce needless expenses related to these products' wastage.

In 1982, Nahmias [43] conducted a review on ordering policies and inventory management of perishable products, considering both deterministic and stochastic demand, being this one of the first reviews on the topic. The author identified two types of perishability, namely fixed lifetime and random lifetime. The former includes the products whose lifetime is previously known and independent of other parameters. The latter refers to products whose lifetime is assumed to be a random variable with a probability distribution. The application of the proposed models to blood bank management is included. Karaesmen et al. [44], in 2010, have also conducted a study in supply chain management of perishable products, taking into account supply and demand. The authors highlighted models where there was inventory level control.

The blood supply chain (BSC) is a particular case of both healthcare and perishable supply chains. Given the context of the importance of supply chain management application to the healthcare area and perishable products, the following sections will focus on the works developed so far on the blood supply chain.

3.2 Blood Supply Chain

The study of the blood supply chain started early in the 1960s. A substantial part of the related literature was developed in the 1970s and 1980s, with several reviews covering distinct aspects and echelons of the BSC being published [4].

In 1973, Jennings [45] presented the first framework for the analysis of the whole blood inventory problem, showing the impact of the application of different inventory policies. In 1976, Cumming et al. [46] presented one of the earliest studies concerning the collection echelon of the BSC. The authors developed a blood collection planning model to eliminate shortage and oversupply of blood. Deuermeyer and Pierskalla [47], in 1978, presented one of the first works in production components. The authors developed an analytical model to minimize the production costs of RBC and platelets. In 1980, Prastacos and Brodheim [48] developed a model to reallocate the blood inventory of several hospitals in a region. The model aimed to reduce the transhipments considering pre-scheduled deliveries, and rotation and retention policies based on blood's age. Later, in 1982, Pratt and Grindon [49] compared different collection sites configurations for different donor arrival rates using a simulation approach. As previously mentioned, and also in 1982, Nahmias [43] developed a review of perishable inventory policies. In 1983, Katz et al. [50] developed a simulation model of platelet production and distribution, based on historical demand. In 1996, James and Matthews [51] studied factors that affect the motivation of donors. A donation cycle framework was developed to analyze blood donor return behavior. More recently, Stanger et al. [52] also addressed the inventory management problem in the BSC, conducting a complete overview on the topic. The article published in 2012 describes the best practices in the platelets inventory management at hospitals, in the United Kingdom, based on the literature and historical data. Lowalekar and Ravichandran [53], in 2013, analyzed the most recent contributions in the area of blood bank inventory management and compare them with the challenges in India's blood banks, identifying research gaps.

The first complete review of the literature on inventory and supply chain management of blood products was presented by Beliën and Forcé [5] in 2012. The authors identified 8 different criteria to classify the existing papers published up to 2010: blood product, solution method, hierarchical level, type of problem, stochastic and deterministic approaches, exact vs heuristic, performance measures, and case studies. They have found an increase in studies on red blood cells and platelets. Considering the solution method, the authors found that most papers used soft computational approaches, such as simulation or statistical analysis, rather than hard computational approaches like integer programming and stochastic programming. Moreover, papers were found to focus more on the hospital level or on the regional blood center level, while the supply chain level was barely studied. Most of the literature on blood supply chain proposes stochastic programming models but insufficient literature exists on the strategic facility location decisions. The study found that the most used performance measures are outdates and shortages, and it was noticed that most papers include practical implementations and/or case studies.

In 2015, Osorio et al. [4] conducted a more recent review of the literature where they evaluate papers from 1963 to 2014 according to operational processes and their parameters. The authors separated the reviewed papers in five sections, defined as the four echelons of the blood supply chain separately: collection, production, inventory and delivery, plus an integration of all echelons. They found that the majority of papers only consider one echelon of the blood supply chain, not addressing the relationships between stages. The authors defend there is a need to model the whole process flow in the blood supply chain. Modeling all BSC echelons can help in the identification of bottlenecks as well as the evaluation of policies from a whole-system perspective.

Three hierarchical levels of decision exist: strategic, tactical, and operational. According to Osorio et al. [4], strategic-level decisions include location decisions, and capacity and staff definition. These decisions have a long-term impact on the BSC because they will affect other lower-level decisions. Below

the strategic level is the tactical level, which is aimed at middle-term planning. Tactical level decisions comprise policy definitions such as inventory policies, planning of collection campaigns, routing and allocation, production master plans, and facilities layout. The operational level refers to decisions that must be made daily. This lowest level comprises decisions related to daily quantities to order, what specific products should be issued to fulfill demand, transshipments between different points, decisions on collection methods, and scheduling of staff and vehicles.

Pirabn et al. [54] reviewed and analyzed the most recent literature on blood supply chain. The study considers papers from 2005 to 2019, and presents a new taxonomy with higher level of detail. The analyzed papers were classified based on the decision-making and forecasting environments, network structure and characteristics of the BSC, type of problems or planning decisions, and modeling technique. Considering the decision-making and forecasting environments, the authors have observed that most papers handle uncertainty and only few deal with deterministic parameters. Most papers were found to only consider one or two echelons but the authors argued that it is necessary to study the multiple echelons of the supply chain, in order to better manage cooperation and coordination between echelons and minimize the influence of supply and demand uncertainty. They noticed that testing and processing steps were the least studied in the analyzed literature while inventory management is the most studied process. The authors detected that despite ABO-substitution being very important in BSC management, only a few papers considered it. Moreover, a trend was found towards considering more complex and integrated problems, such as decision-making environments, and multi-echelons, among others.

These review papers reported a variety of problems related to the BSC. The following section will address in more detail the studies that are more relevant for the present work, separating them by the solution method used.

3.3 Solution Methods

Blood supply chain problems have been analyzed using a wide range of different methodologies. Some of the most popular solution methods in the literature are simulation [8, 55–57], dynamic programming [58], and integer programming [1, 59]. These approaches can be combined with other methods to study real-life problems. Furthermore, models cover different aspects of the blood supply chain and indicate a variety of decision variables, objective functions, and constraints, depending on the problem to be studied.

3.3.1 Integer Programming

A linear-programming problem is the problem of either minimizing or maximizing a linear objective function subject to a finite set of linear constraints, as defined by Cormen et al. [60]. Let n denote the number of variables, and m denote the number of constraints. Let $x_1, ..., x_n$ denote the n variables in the linear program. Let $c_1, ..., c_n$ denote the coefficients of these variables in the objective function. Let A_{ij}, $i = 1, ..., m$ and $j = 1, ..., n$ denote the coefficient of x_j in the ith constraint. Considering that A denotes the matrix (A_{ij}), c denotes the vector $(c_1, ..., c_n)$, and x the vector $(x_1, ..., x_n)$, the linear programming problem can be defined as

$$\begin{aligned} &minimize && c^T x && \\ &subject\ to && Ax && \leq b \\ & && x && \geq 0, \end{aligned}$$

where b is a vector of constants.

An integer linear-programming (ILP) problem is a linear-programming problem where the variables x must take on integer values, i.e., $x \in Z$. When some variables, not all, are not constrained to be integer, it is said that we have a mixed integer linear programming.

Linear-programming can be used to solve a variety of problems from finding shortest paths to calculating max flows. In fact, linear-programming can be applied to any type of problem that aims to minimize or maximize a certain objective, given limited resources as long as the objective can be specified as a linear function of variables and the constraints on resources can be specified as inequalities or equalities in those variables.

The first-ever study conducted on the Portuguese BSC was published by Araújo et al. [7] in 2020. The authors proposed an ILP model for both tactical and operational planning of the BSC while minimizing costs, waste, and dependence on other regions. This work studied the flow of blood from the collection, production, and consumption at demand points. The proposed model considered multi-products, inventory at main centers and hospitals, perishability, blood groups, and waste of blood, and its derived products. Due to the model's complexity, a two-stage solution approach was developed, with the first stage dealing with tactical decisions by providing facility allocations, and the second stage addressing operational decisions using these allocations as input. The model provided a solution with lower waste and purchase values, demonstrating there is room for improvement in these areas. The authors suggested this improvement could be accomplished through a more fair distribution of activities among the main centers and optimizing the allocations of facilities. Neither stochasticity in supply nor demand was considered in the proposed model.

Several papers in the literature use mixed integer linear programming (MILP) modeling approaches, such as in Zahiri et al. [14], Ramezanian and Behboodi [61], Zahiri and Pishvaee [62], and Sha and Huang [63], to analyze different BSC aspects such as the optimal location for collection points or the allocation of donors to the established collection points, having specific goals and considering several blood characteristics. Indeed, all these papers addressed the location-allocation problem, in which the goal is to determine an optimal number and location for a set of new facilities to satisfy customer's demand and minimize the transportation cost from facilities to customers [64].

Zahiri et al. [14] proposed a MILP model to make strategic and tactical decisions for a blood collection system. The proposed model determines the optimal number and locations of main and temporary blood bank facilities over the planning horizon, and it assigns donors to the established facilities in each period with the goal of minimizing total costs (i.e., costs of opening blood collection facilities; costs of relocating temporary facilities, and blood shipment costs). Regarding tactical decisions, the volume of blood shipped from temporary blood facilities to main centers is determined. Due to the model's uncertainty, a robust possibility programming approach was developed. This approach recognizes uncertainties both in the objective function and constraint coefficients. The obtained results demonstrate the superiority of the robust possibility approach over other methods. The authors proved the applicability of the proposed model with data from a real case study in Iran.

The purpose of the study conducted by Ramezanian and Behboodi [61] was to increase utility and motivate donors to donate blood. This research presents a blood supply chain model that minimizes the supply chain costs while determining optimal locations for blood facilities and allocating donors to those facilities based on a blood donors' utility function. The suggested model is expanded using robust optimization approaches to include uncertainty. This study considers blood donors' effect on blood supply chain by looking at the distance between donors and facilities, advertising budget in facilities and blood donors' experience factor in facilities. The authors proposed a MILP model to define the problem. The most important result obtained by the proposed model was that blood donors are assigned to near facilities in order to walk or drive shorter distances. Also, blood donors are more attracted to facilities with higher experience factor for donors.

Zahiri and Pishvaee [62] presented a location-allocation bi-objective MILP with the aim of minimizing the total blood supply chain costs as well as the shortages. The first objective minimizes the total cost while the second objective minimizes the maximum unmet demand. Two robust possibilistic approaches were developed due to the uncertain nature of some crucial input parameters. The applicability of the model was demonstrated by a real case study in Iran. The obtained numerical results showed the superiority of the proposed robust possibilistic programming models with significant cost savings when compared to the current existing blood supply chain network in the considered case study. The proposed model considers blood substitution and stochastic supply and demand, but does not consider inventory levels. Arvan et al. [65] developed a study to locate components in a network and allocate them to each other. The components considered were donation sites, testing and processing labs, blood banks, and demand points. A bi-objective MILP model was proposed with the aim of minimizing total costs as well as the time that blood products remain in the network. Again, despite considering the perishable nature of blood components, the inventory echelon is not included in the model, as perishability is obtained through transportation and processing times.

Sha and Huang [63] developed a MILP location-allocation model for the supply of emergency blood in the impact of earthquakes in Beijing with the goal of minimizing the total costs over the planning horizon. The proposed model was designed based on the Lagrangian relaxation method. In contrast with Zahiri and Pishvaee [62], Sha and Huang [63] accounted for inventory levels but neither blood substitution or stochastic supply and demand were considered.

Alfonso and Xie [66] and Alfonso et al. [67] presented mathematical models for blood collection planning. In the former study [66], the objective is to determine weeks of collection at each mobile site to ensure the regional self-sufficiency of the blood supply over a yearly planning horizon. The model optimizes the quantity of blood to be collected each week. The second paper [67] incorporates detailed weekly planning to determine days of collections at each mobile site for the same self-sufficiency objective. In both papers, two MILP models are proposed, and their efficiency is assessed with field data from the French Blood Service. These models consider important features, such as the regional donation capacity, donor generosity, and donor availability, but none of the models addressed blood substitution.

Gunpinar and Centeno [1] and Hemmelmayr et al. [59] proposed integer linear programming (ILP) models. Gunpinar and Centeno [1] presented integer programming models addressing inventory problems in a hospital blood bank with the goal of minimizing the total cost, shortage, and wastage levels of blood products at a hospital during the planning horizon. The authors focused on the red blood cells and the platelets components of the whole blood cells. The proposed models include non-linear constraints to which a linearization technique is applied to replace them with linear constraints. The study uses stochastic programming to examine demand uncertainty. The stochastic integer programming models consider age of blood units on inventory and the demand for two types of patients (one requiring fresh blood). In their formulations, the crossmatch-to-transfusion ratio (C/T) and the crossmatch release period are also considered. The incorporation of the C/T ratio allows the model to represent the real-world problem more precisely. However, that modification required the use of a simpler deterministic version of the model instead of the original stochastic version, due to computational issues, as noticed by the authors. The authors were able to model perishability and also considered more than one blood product.

Hemmelmayr et al. [59] used ILP to solve the problem of delivering blood products to Austrian hospitals to minimize the cost of both delivery and spoilage. They develop and evaluate two alternative delivery strategies, having in the mind the fact that, for practical reasons, regularity in delivery patterns is preferable. The first strategy retains the concept of regions and the use of fixed routes, and uses IP techniques to optimally decide delivery days. The second strategy combines more flexible routing decisions with a focus on repeating delivery patterns for each hospital, and it is based on viewing the problem as a periodic vehicle routing problem (PVRP) with tour length constraints. A variable neighborhood search

algorithm was developed for the solution of this variant of the PVRP. The authors compared the current vendee-managed inventory set up with a vendor-managed inventory system. The applicability of the approach was demonstrated by testing it on real data from Austrian blood bank.

3.3.2 Two-Stage Stochastic Programming

Two-stage stochastic programming is also a very common methodology in the reviewed literature. In these models, decision variables are divided into two groups: first-stage decisions and second-stage decisions (Birge and Louveaux [68]). The first-stage decisions are independent of the uncertainty and must be defined earlier than the realization of the uncertainty while the second-stage decisions are dependent on the uncertainty and are defined after the uncertainty is disclosed [68]. This methodology was used in Jabbarzadeh et al. [69], Fahimnia et al. [70], Hamdan and Diabat [71], Dillon et al. [72], and Hosseini-Motlagh et al. [2] to address different problems concerning the BSC.

Both the studies conducted by Jabbarzadeh et al. [69] and Fahimnia et al. [70] addressed the challenge of getting supplies to people affected by disasters, as the work developed by Sha and Huang [63] presented before. Jabbarzadeh et al. [69] presented a robust network design model for determining blood facilities location-allocation decisions for multiple post-disaster periods, addressing uncertainties in blood demand and supply. The model aims to minimize the total cost of delivering blood products to hospitals while ensuring the network is robust. The model accounts for decisions such as location and number of permanent and temporary facilities, allocation of donors, amounts of blood to be collected, and inventory. A more recent research in disaster context was developed by Fahimnia et al. [70] who presented a bi-objective stochastic model to design a blood supply chain network in disasters. The first objective minimizes the supply chain costs and the second objective minimizes the average blood delivery time from mobile blood facilities to hospitals. They formulate a hybrid solution approach, combining the ϵ-constraint and Lagrangian relaxation method. The proposed model determines inventory levels, the number and allocation of mobile blood facilities and the volume of collected blood to be shipped. Neither the models proposed by Jabbarzadeh et al. [69] nor Fahimnia et al. [70], nor Sha and Huang [63] considered blood substitution despite being this a characteristic with a giant impact on the BSC, especially in disaster situations.

Hamdan and Diabat [71] presented a two-stage stochastic programming model for a red blood cells supply chain that simultaneously accounts for the production, inventory, and location decisions under demand uncertainty. The model considers four levels: mobile blood facilities, local blood banks, regional blood banks and hospitals, as well as the truckload transportation, the uncertainty of supply and demand, the integration of inventory and distribution decisions, the perishability of blood units, and the blood type substitution. The proposed model focuses on reducing the number of outdates, the system costs, and blood delivery time. The model was solved by applying the ϵ-constraint method and its applicability was demonstrated with a real case study from The Hashemite Kingdom of Jordan.

Dillon et al. [72] proposed a two-stage stochastic programming approach to support the management of the blood inventory in hospitals considering uncertain demand and blood type substitution, but do not consider stochastic supply. This work addressed the considered problem similarly to Gunpinar and Centeno [1] however, this approach is more strategic, using two-stage stochastic programming. The goal is to define a RBC optimal inventory control policy for the BSC based on periodic review, in which the authors aim to determine the optimal time between inventory reviews (R) and the target inventory level (S). It is proposed a model for defining optimal (R,S) inventory control policies that is able to take into consideration the perishable nature of blood while representing the complex stochastic nature of blood demand. The inherent problem consists in defining an ordering rule that should be followed by the hospital's inventory management team that is based on a predefined periodic review (R) and an inventory

reference level to be used as a target for each blood type. The purpose of the model is to define the optimal parameters (R,S) in terms of costs, taking into account the constraints required by the problem's nature, like product perishability. The applicability of the proposed approach was demonstrated using a case study.

Hosseini-Motlagh et al. [2] proposed a two-stage stochastic programming model for managing a RBC supply chain considering blood perishability, blood ABO-Rh(D) compatibility, and demand uncertainty. In the first stage of the model, tactical decisions are determined, such as the location and number of mobile blood facilities, and in the second stage inventory and production decisions are taken. The model determines the optimal location-allocation and inventory management decisions and aims to minimize the total cost of the supply chain.

3.3.3 Simulation

Pierskalla [55] presented one of the most widely read papers in the area of blood supply chain management [5]. The study described an overview of models for assigning donor areas and transfusion centers to community blood centers, determining the number of community blood centers in a region, establishing their locations, and coordinating supply and demand. Also, the author described tactical and operational models targeting blood collection and allocation to hospitals, inventory management, blood delivery and cross-matching. The study revealed that a centralized community blood center is more efficient than a decentralized system. A simulation model and statistical analysis was used to develop a target inventory decision function for inventory levels at an independent hospital blood bank (HBB), at HBBs that are a part of a centralized system and at the community blood center.

Katsaliaki et al. [8] presented a discrete-event simulation to determine policies for managing the blood inventory system in order to reduce shortages and wastage, increase service levels and safety procedures, and reduce costs. The proposed model captures the entire supply chain, from donation to transfusion. The authors presented a case study for a medium-size hospital in the UK to demonstrate the applicability of the model. Similarly, Haijema et al. [56] and Duan and Liao [57] used simulation approaches. Haijema et al. [56] proposed a model that combines Markov dynamic programming and a simulation approach for a Dutch blood bank. Their focus was on inventory management of platelets and production costs. Duan and Liao [57] proposed a simulation-optimization approach to determine optimal policies. The model considers stochastic supply and demand.

Lowalekar and Ravichandran [73] developed a simulation model to compare different collection policies. One of the major conclusions of this work is that a policy of collecting as much blood as possible may lead to high wastages without a meaningful reduction in shortages. Afonso et al. [74] also developed a simulation model considering the collection echelon. The model aimed at determining the best configurations of human resources and donor appointment strategies.

3.3.4 Other Methods

Nagurney et al. [75] developed the first model that uses mathematical programming to optimize the entire blood supply chain, considering collection points, testing/processing locations, storage facilities, distribution centers and points of demand, representing the entities of all echelons of the supply chain as well as their relations. The model considers the blood supply chain as a network problem, defining different nodes and arcs that represent the supply chain entities and their relationships. The model does not consider blood group types.

Heidari-Fathian et al. [76] presented a mathematical model for designing a reliable blood supply chain network with the sole objective of cost minimization. Three types of blood collection facilities were

considered at the collection echelon and blood perishability is covered. A numerical example was used to prove the applicability of the proposed model.

Fazli-Khalaf et al. [77] proposed a tri-objective mathematical model to design a blood supply chain in emergency situations. The objectives of the proposed model were to minimize total costs, transportation times and maximize total testing reliability. Both different transportation means, with variant speed and capacity, and testing laboratories' technologies were considered in the model. Habibi-Kouchaksaraei et al. [78] developed a bi-objective multi-period blood supply chain network with the goals of minimizing both costs and shortages of blood. Three echelons of supply, processing and distribution were considered. The model aimed to determine the number and location of facilities and their allocation under disaster situations.

3.4 Summary

In this chapter, it is presented the most relevant literature related to the BSC, along with the description of some important concepts for the understanding of the problem in question, such as the concept of supply chain management and its application to healthcare.

From the above reviewed literature, blood products' perishability and red blood cell substitution are characteristics not considered in most of the papers, since these characteristics increase the complexity of the proposed models. Based on the analyzed literature, Araújo et al. [7], Dillon et al. [72] and Hamdan and Diabat [71] were the only authors that modeled both characteristics. However, some other authors were able to model blood products' perishability not considering blood substitution, such as in Haijema et al. [56], Gunpinar and Centeno [1], and Duan and Liao [57]. The models that do not consider these characteristics, like in Zahiri et al. [14], Alfonso and Xie [66], Alfonso et al. [67], Hemmelmayr et al. [59], Fahimnia et al. [70], Sha and Huang [63], Jabbarzadeh et al. [69], and Ramezian et al. [61], might not be viable when certain patients cannot use the collected blood, ending up with the blood being stored or even discarded.

Gunpinar and Centeno [1], Hemmelmayr et al. [59], Jabbarzadeh et al. [69], Fahimnia et al. [70] and Zahiri et al. [14] considered uncertain parameters but none considered the impact of blood donors in the supply chain design.

Tables 3.1 and 3.2 summarize the main characteristics of the analyzed papers.

Based on the studied literature and considering that the problem to be studied concerns the collection echelon of the BSC, the methodology adopted for the development of this work is an optimization model based on integer programming. The different blood components will not be considered in the proposed model, as the focus of the work is the whole blood collected in the collection stage. Thus, red blood cell substitution is a characteristic not addressed. The perishable nature of blood is also not considered due to the added complexity of the model. The chosen methodology is further detailed in the following chapter.

Table 3.1: Literature classification by modelling technique.

References	ILP [a]	MILP [b]	TSSP [c]	Simulation	Variational Inequality
Araújo et al. [7]	✓				
Zahiri et al. [14]		✓			
Ramezanian et al. [61]		✓			
Zahiri and Pishvaee [62]		✓			
Sha and Huang [63]		✓			
Alfonso et al. [67]		✓			
Alfonso and Xie [66]		✓			
Gunpinar et al. [1]	✓				
Hemmelmayr et al. [59]	✓				
Fahimnian et al. [70]			✓		
Jabbarzadeh et al. [69]			✓		
Hamdan and Diabat [71]			✓		
Dillon et al. [72]			✓		
Hosseini-Motlagh et al. [2]			✓		
Pierskalla et al. [55]				✓	
Katsaliaki et al. [8]				✓	
Nagurney et al. [75]					✓
Proposed Model	✓				

[a] Integer Linear Programming
[b] Mixed Integer Linear Programming
[c] Two-Stage Stochastic Programming

Table 3.2: Modeled features of the analyzed models.

References	Whole Blood	Red Blood Cells	Multi products	Inventory Decisions	Stochastic Demand	Stochastic Supply	Blood Substitution	Blood Collection	Blood Distribution
Araújo et al. [7]			✓	✓			✓		✓
Zahiri et al. [14]	✓				✓	✓		✓	
Ramezanian et al. [61]	✓				✓	✓		✓	
Zahiri and Pishvaee [62]	✓				✓	✓	✓	✓	
Sha and Huang [63]	✓			✓				✓	✓
Alfonso et al. [67]		✓						✓	
Alfonso and Xie [66]		✓						✓	
Gunpinar et al. [1]			✓	✓	✓				
Hemmelmayr et al. [59]	✓								✓
Fahimnian et al. [70]		✓		✓	✓	✓		✓	✓
Jabbarzadeh et al. [69]	✓				✓	✓		✓	
Hamdan and Diabat [71]		✓		✓	✓	✓	✓		
Dillon et al. [72]		✓		✓	✓		✓		
Hosseini-Motlagh et al. [2]		✓		✓	✓		✓	✓	✓
Pierskalla et al. [55]	✓			✓				✓	✓
Katsaliaki et al. [8]		✓		✓	✓	✓	✓		
Nagurney et al. [75]		✓		✓	✓	✓		✓	✓
Proposed Model	✓							✓	

Chapter 4

ILP Formulation to Optimize Blood Collections

The previous chapters provided the context needed to develop the optimization model that is described in this chapter. A brief description of the data provided by IPST is presented to better characterize the problem to be studied. A detailed description of the problem and its relevant aspects is also carried out. Furthermore, the mathematical formulation for the problem described is presented, including sets, parameters, model variables, constraints, and the objective function, along with an additional formulation considering more aspects of the BSC.

4.1 Data

This section describes the data that was made available by IPST, allowing the formulation of the model presented below.

The data provided corresponds to the period between January 1990 to August 2020 and refers to blood donations registered by IPST in this period. Each of the three main centers, namely CSTL, CSTP, and CSTC, independently organizes its blood collections, and consequently, each main center records its data concerning the donations. The data provided by IPST include all blood collection records registered by all main centers. Data was made available on nearly 6 million blood donation records.

Figure 4.1 illustrates the available records' distribution over the last ten years for each main center. Considering the number of records registered by IPST, it can be seen in figure 4.1 that there is a similar behavior between the three main centers once, over the years, the decrease in the number of records is uniform regardless of the main center, except for a few instances. Moreover, the data shows that the CSTP and CSTL are the main centers with more registered donations in the last eight years, while in 2010 and 2011, it was the CSTC that had the highest number of registered records. By analyzing the years 2017, 2018, and 2019 (see table 4.1), it is possible to see a slight decrease in the number of donations registered over time. However, as 2019 is the year with the most recent data in a pre-pandemic period and the decline of the year 2019 compared to previous years is not that pronounced, the data from 2019 was used for evaluation purposes.

Table 4.1: Number of IPST registered donations in the last three years.

	2017	2018	2019
Number of donations	248 905	239 684	233 783

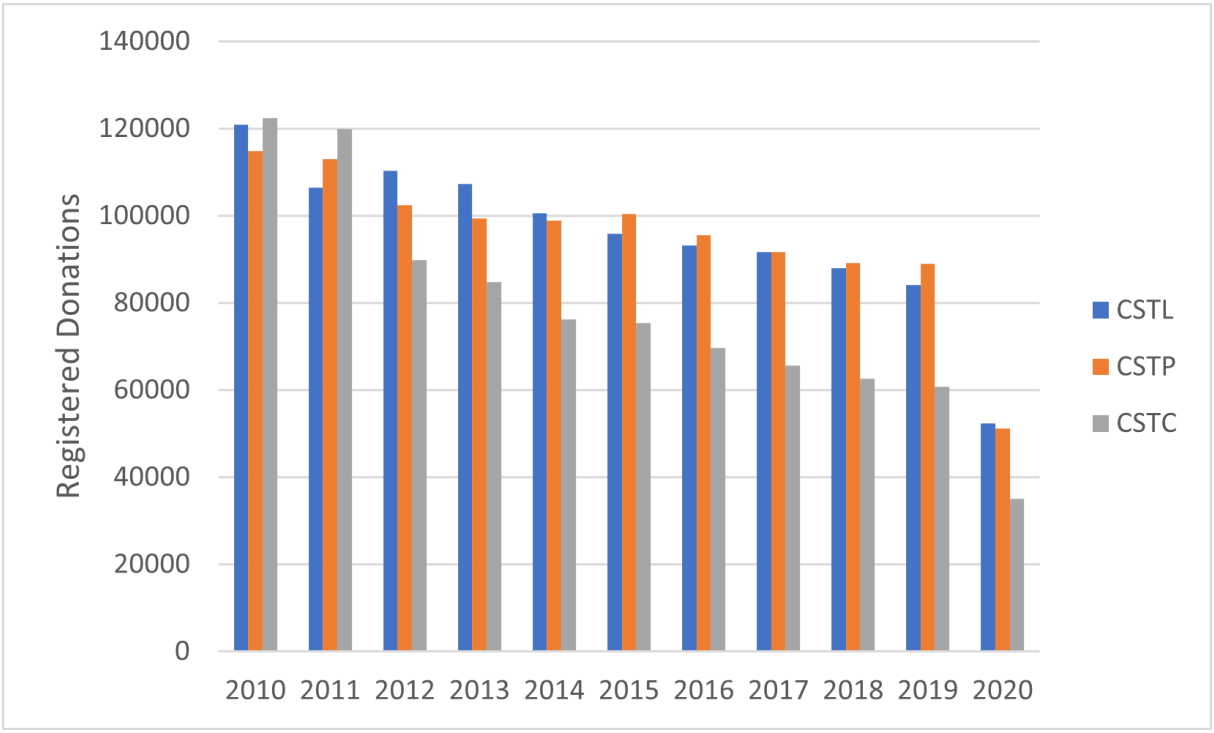


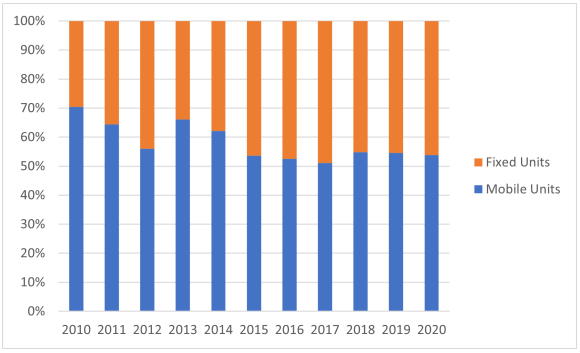
Figure 4.1: Distribution of the available records over the last ten years per main center.

Regarding the information about the donation, the following is registered: the place of the collection identified by district, county, and postal code, the date, the type of collection facility - whether it is a mobile unit or a fixed station -, the facility identification number, the main center that is associated with that collection point, the distance (in kilometers) from the main center to the collection site, the type of collection - whether it is apheresis or not -, the number of expected donors and those who appeared, among others. In total, 58 features are registered per donation record, of which 16 concern donors' personal information while the other 42 features are related to the collection and its secondary effects on donors.

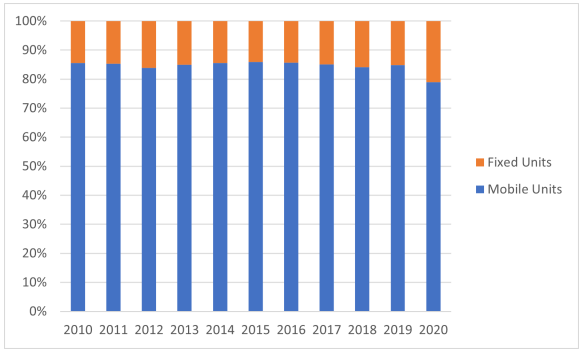
By analyzing the provided data concerning the type of collection facility - whether it is a mobile unit or a fixed station -, it is possible to realize where had been made more donations over the last ten years for each main center. Figure 4.2 illustrates this information for the CSTL, CSTP, and CSTC, respectively, figures 4.2a, 4.2b, and 4.2c. It can be seen that, depending on the main center, the donors have different behaviors since, at first sight, a difference between the graphics is visible.

Looking in more detail at each main center individually, it can be concluded that each main center presents a uniform behavior over the last years. Considering first the CSTL, figure 4.2a, it can be seen that more than 50% of the registered donations occurred in mobile units, with the fixed points still representing a considerable portion of total donations. For the CSTP, the situation is different. Looking at figure 4.2b, it is possible to see that more than 80% of the records represent donations in mobile units (except for the year 2020), meaning that the donations in fixed facilities represent less than 20% of the total records for the CSTP. This disparity in values can be justified by the fact that not all collection sessions organized by the CSTP are reported to IPST, and as the provided data only refers to donations organized by IPST, there may be more data besides these on CSTP donations, and therefore, this information may not fully represent reality. For the CSTC, figure 4.2c shows that more than 60% of the donations were in mobile units, with recent years demonstrating a slight downward trend in the number of registered donations in those units.

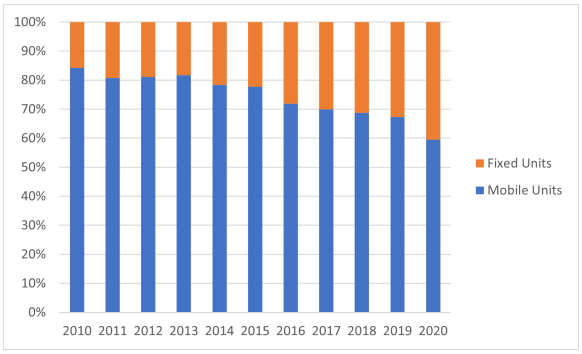
The locations for establishing mobile blood collection facilities were obtained from the data and



(a) CSTL



(b) CSTP



(c) CSTC

Figure 4.2: Distribution of the available records per type of collection facility for each main center over the last ten years.

include places such as universities, fire stations, churches, or companies, among others. Hospitals are considered permanent blood collection facilities, but they do not exist in all counties of Portugal. Moreover, from the existing hospitals, not all have blood collection services, which is one of the reasons contributing to the establishment of mobile blood collection facilities across the country. From the data provided, the values for the distances between the collection points, both mobile and permanent, and the main centers were obtained.

From the available data, it was noticed that IPST has two different types of mobile blood collection facilities. These facilities do not have a permanent location because they are scheduled for a particular day at a specific location to collect the blood from the donors, meaning these facilities are moved from one location to another for the collections. The first one involves the movement of a multidisciplinary team and vans equipped with all the material required for the blood collections. The other type of mobile facilities does not imply the displacement of equipped vans. In these cases, the equipment needed for blood collection is unloaded in an existing building, and a temporary facility is created. From the model point of view, these two types of mobile blood units have the same behavior, as donors move there to donate blood, and then, the blood is shipped from the collection point to the main center, meaning that all model constraints presented below regarding mobile blood facilities will be applied to both types for evaluation purposes. The main difference between them is in the cost of moving these facilities from one location to another, with those that involve moving equipped vans having higher costs than those that do not move them. Each mobile blood collection facility has a different identification number associated that allows it to be distinguished from the others.

Every day, the blood supply chain processes thousands of units of whole blood and its derivative products, including dozens of collection locations and even more demand zones, causing the study of the blood supply chain a challenge. From the available data, it was possible to understand what is done in

the first echelon of the BSC and which entities are involved, realizing how blood collections are organized. Based on the data provided, a mathematical model was formulated to describe the collection echelon of the BSC. In the following section, a detailed description of the problem in hands is presented.

4.2 Problem Description

In the BSC network, several decisions must be accounted for on all three levels: strategic, tactical, and operational. The problems and decisions here addressed are comprised in the first (strategic) hierarchical level. Particularly, they are associated with the planning level, as the focus of this work is the collection of blood. The underlying problem is therefore determining where the mobile blood collection facilities should be located and when they should be moved to guarantee that the blood demands are fulfilled while BSC total costs are minimized. To do so, an integer programming (IP) approach is adopted.

The choice of using IP to model the problem in hands is because these approaches were widely used to study this kind of problem, based on the analyzed literature, and are easy to extend if there is the need to consider more objective functions or add new constraints.

As previously mentioned, the focus of this work is the first echelon of the BSC, the collection stage, not addressing with much detail the remaining echelons. The decision of not focusing on the other echelons is related to the purpose of this thesis, which is the optimization of blood collections planning. It is necessary to clarify that this decision is also related to the fact that the data made available only concerns the blood collections, not including information about the remaining echelons of the BSC.

The supply chain network considered in this study comprises blood donor zones, blood collection facilities - permanent and mobile -, and main blood centers. Donors can donate blood at either permanent or mobile blood facilities within a certain geographical distance, but not at main blood centers. The location of mobile blood facilities can vary over the planning horizon, while the location of permanent blood facilities must be settled at the beginning of the planning horizon and should not change during the planning horizon. The blood collected at blood facilities, both permanent and mobile, is shipped to main blood centers, at the end of each period. The main blood centers process the blood to obtain its derivative products and perform the necessary tests to determine blood type and test for known diseases. The blood components are stored at specific conditions until they are shipped to hospitals and health centers according to their demand needs. The flow of blood between the main centers and the demand zones is not considered in the developed model, as this flow is not the main purpose of this work, and as mentioned above, data regarding this flow was not available nor related to the blood consumption at the demand zones. Thus, the three last echelons of the BSC, namely production, inventory, and distribution, were not considered in the model formulated below.

The objective is to minimize the total supply chain costs, including the cost of relocating mobile blood facilities in consecutive periods and transportation costs, while ensuring that the blood demands are fulfilled. At each period of the planning horizon, the proposed model aims to determine the number of needed mobile blood facilities, the optimal location of those facilities, the allocation of donors to the established blood facilities, and the amount of blood required for collection at each facility.

Moreover, the following assumptions are considered in the proposed model:

- The BSC is single product (whole blood);
- The location of main centers and permanent blood collection facilities is given;
- The number of donor groups is the number of counties in Portugal and the center point of each county is used for distance calculations;

- The storage capacity of collection facilities and main centers is limited;
- All mobile blood collection facilities have the same storage capacity, which is smaller than the storage capacity of permanent collection facilities, which in turn is smaller than the main blood centers capacity;
- All mobile blood collection facilities are initially located at the main centers.

A mathematical formulation for the above-mentioned description is presented in the following section.

4.3 Core Mathematical Formulation

In this section, the mathematical formulation of the model is presented. Figure 4.3 displays a small running example parameterized with the notation described below, which will be used to show the applicability of the proposed formulation. The example consists of two donor groups (DG1, DG2), two mobile blood collection facilities (MF1, MF2), one main center (MC), and two possible locations to establish collection points (A and B).

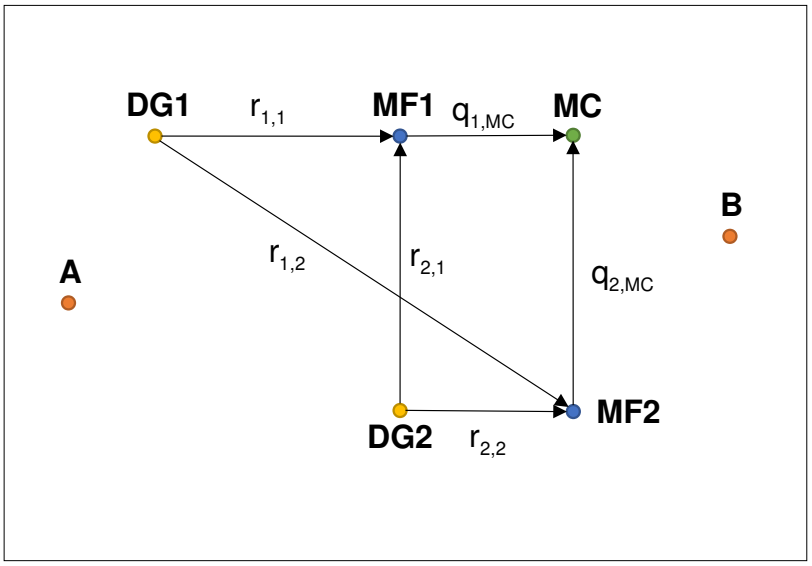


Figure 4.3: Running example parameterized with the model's notation.

The sets, parameters, and decision variables are detailed below. Parameters are constant values and, for notation clarity, lower-case letters are used to represent them and capital letters to represent decision variables. The notation is described as follows:

Sets	
I	set of donor groups $(i = 1, ..., I)$
J	set of possible locations for mobile blood facilities $(j = 1, ..., J$ and $j_1, j_2 \in$ J)
K	set of main blood centers $(k = 1, ..., K)$
L	set of permanent blood facilities $(l = 1, ..., L)$
T	set of time periods $(t = 1, ..., T)$
W	set of week periods $(w = 1, ..., W)$

continue on next page

Parameters

Uncertain parameters

c_{j_1,j_2}	cost of moving a mobile blood facility from location j_1 to j_2
c_{jk}	transportation cost per unit of blood between the mobile facility located at j and the main blood center located at k
c_{lk}	transportation cost per unit of blood between the permanent facility located at l and the main blood center located at k
r_{ij}	distance between donor group i and the candidate mobile blood facility located at j
w_{il}	distance between donor group i and the permanent blood facility located at l
q_{jk}	distance between the candidate mobile facility located at j and the main blood center located at k
q_{lk}	distance between the permanent blood facility located at l and the main blood center located at k
v_{it}	maximum donation capacity of donor group i in period t
D_t	blood demand (in blood pack units) in period t

Deterministic parameters

P_k	number of mobile blood facilities in the main center located at k
r_0	maximum coverage radius of mobile blood facilities; if $r_{ij} \leq r_0$, i is covered by j
w_0	maximum coverage radius of permanent blood facilities; if $w_{il} \leq w_0$, i is covered by l
q_0	maximum coverage radius of main blood centers; if $(q_{jk} \vee q_{lk}) \leq q_0$, j or l, respectively, is covered by k
v	maximum transportation capacity (in blood pack units)
v_k	maximum storage capacity (in blood pack units) of the main center located at k
v_l	maximum storage capacity (in blood pack units) of the permanent facility located at l
M	maximum number of collected blood pack units in each period
N	maximum number of allowed mobile blood facilities in weekdays
N'	maximum number of allowed mobile blood facilities in weekend days
A_{kw}	average number of blood pack units for the main center located at k in week w
ω	minimum coverage percentage of total collected blood pack units in each week

Decision Variables

$Y_{j_1,j_2,t}$	a binary variable equal to 1 if a mobile blood facility is located at j_1 in period $t-1$ and moves to location j_2 in period t, and 0 otherwise
Z_{jt}	a binary variable equal to 1 if a mobile blood facility is located at location j in period t, and 0 otherwise
X_{ijt}	a binary variable equal to 1 if donor group i is assigned to a mobile blood facility located at j in period t, and 0 otherwise
X_{ilt}	a binary variable equal to 1 if donor group i is assigned to a permanent facility located at l in period t, and 0 otherwie
X_{jkt}	a binary variable equal to 1 if a mobile blood facility located at j is assigned to a main blood center located at k in period t, and 0 otherwise
X_{lkt}	a binary variable equal to 1 if a permanent blood facility located at l is assigned to a main blood center located at k in period t, and 0 otherwise
Q_{ijt}	the blood volume (in blood pack units) donated by donor group i in a mobile facility located at j in period t

continue on next page

Q_{ilt}	the blood volume (in blood pack units) donated by donor group i in a permanent facility located at l in period t
Q_{jkt}	the blood volume (in blood pack units) shipped from a mobile blood facility located at j to a main center located at k in period t
Q_{lkt}	the blood volume (in blood pack units) shipped from a permanent facility located at l to a main center located at k in period t

The objective function (4.1) minimizes the total cost of moving mobile blood facilities in each period, and the cost of delivering blood from mobile blood collection facilities and permanent collection facilities to main blood centers during the planning horizon.

$$\min \quad \sum_{j_1,j_2,t} c_{j_1,j_2} Y_{j_1,j_2,t} + \sum_{j,k,t} c_{jk} Q_{jkt} + \sum_{l,k,t} c_{lk} Q_{lkt} \tag{4.1}$$

Constraints (4.2) to (4.4) refer to the movement of mobile blood collection facilities in each period. Constraints (4.2) ensure that at most one mobile blood facility can be moved to each candidate location j_2 in each period. Constraints (4.3) ensure that a mobile blood facility can be moved to at most one candidate location in each period. Constraints (4.4) ensure that a mobile blood facility can only be moved to another location (from j_1 to j_2), if in the previous period the facility was relocated to that location (from j to j_1), i.e., a mobile blood facility cannot move from a location where it had not been located. Considering the example depicted in figure 4.3, it is only possible to move to location A, in the same period, or MF1, or MF2, but not both (constraints (4.2)). In the example of figure 4.3, MF1 (or MF2) cannot be moved to both locations A and B in the same period, it can just be moved to one of them (constraints (4.3)). If MF1 is moved from its current location (j) to location A (j_1) in $t = 2$, in $t = 3$ MF1 can be moved from A (j_1) to B (j_2) (constraints (4.4)).

$$\sum_{j_1} Y_{j_1,j_2,t} \leq 1, \quad \forall j_2, t \tag{4.2}$$

$$\sum_{j_2} Y_{j_1,j_2,t} \leq 1, \quad \forall j_1, t \tag{4.3}$$

$$\sum_{j_2} Y_{j_1,j_2,t} \leq \sum_{j} Y_{j,j_1,t-1}, \quad \forall j_1, t \geq 2 \tag{4.4}$$

Each main center, located at k, has a limited number of mobile blood facilities that can be moved in each period, which is assured by constraints (4.5).

$$\sum_{j_2} Y_{j_1,j_2,t} \leq P_k, \quad \forall j_1 = k, t \tag{4.5}$$

Constraints (4.6) ensure the minimal interval of *d* days between two consecutive mobile collections at the same location. For example, if MF1 is moved in day 1 to location A, it can only be moved again to location A in day 15 , considering *d*=14 days.

$$\sum_{j_1,t'=t}^{t+d} Y_{j_1,j_2,t'} \leq 1, \quad \forall j_2, t \leq |T| - d \tag{4.6}$$

Constraints (4.7) to (4.9) define, respectively, the maximum storage capacity of each mobile blood

facility, each permanent facility, and the maximum capacity of main blood centers.

$$\sum_{i} Q_{ijt} \leq v, \quad \forall j, t \tag{4.7}$$

$$\sum_{i} Q_{ilt} \leq v_l, \quad \forall l, t \tag{4.8}$$

$$\sum_{j} Q_{jkt} + \sum_{l} Q_{lkt} \leq v_k, \quad \forall k, t \tag{4.9}$$

Constraints (4.10) restrict the blood volume donated by each donor group in each period. For example, considering that DG1 has 20 donors, there cannot be donated by DG1 more than 20 blood pack units between mobile and permanent facilities in each period.

$$\sum_{j} Q_{ijt} + \sum_{l} Q_{ilt} \leq v_{it}, \quad \forall i, t \tag{4.10}$$

Constraints (4.11) and (4.12) ensure that all blood volume collected at each mobile blood facility and at each permanent facility, respectively, is delivered to main centers in each period.

$$\sum_{i} Q_{ijt} = \sum_{k} Q_{jkt}, \quad \forall j, t \tag{4.11}$$

$$\sum_{i} Q_{ilt} = \sum_{k} Q_{lkt}, \quad \forall l, t \tag{4.12}$$

Constraints (4.13) to (4.16) guarantee the coverage restrictions between mobile and permanent facilities and main centers, between donors and mobile facilities, and donors and permanent facilities. Constraints (4.13) assure that a mobile blood facility located at j can be assigned to the main center located at k, if it is covered by the main facility's coverage radius ($q_{jk} \leq q_0$) and there is a mobile blood facility in location j. The same applies to constraints (4.14) considering permanent facilities and main centers. Constraints (4.15) ensure that a group of donors i can only be assigned to a mobile blood facility located at j if there is a mobile blood facility in that location and the donor is within the coverage radius ($r_{ij} \leq r_0$). The same applies to constraints (4.16) between donors and permanent facilities. Considering the example presented in figure 4.3 and $q_0 = 50$ km, and $q_{1,MC} = 15$ km, which is the distance between MF1 and MC, MF1 located at its current position (j) is assigned to the main center MC because $q_{1,MC}$ is smaller than 50 km, just like MF2. Considering now $r_0 = 25$ km, $r_{1,1} = 15$ km, and $r_{1,2} = 30$ km, being $r_{1,1}$ and $r_{1,2}$ the distance between DG1 and MF1, and MF2, respectively, and $t = 1$. DG1 is assigned to MF1 and not to MF2 because the distance between DG1 and MF2, $r_{1,2}$, is higher than the maximum coverage radius, r_0.

$$X_{jkt} q_{jk} \leq q_0 Z_{jt}, \quad \forall j, k, t \tag{4.13}$$

$$X_{lkt} q_{lk} \leq q_0, \quad \forall l, k, t \tag{4.14}$$

$$X_{ijt} r_{ij} \leq r_0 Z_{jt}, \quad \forall i, j, t \tag{4.15}$$

$$X_{ilt} w_{il} \leq w_0, \quad \forall i, l, t \tag{4.16}$$

Constraints (4.17) and (4.18) prevent collecting blood at mobile blood facilities and permanent facilities, respectively, from donors not assigned to those facilities. Constraints (4.19) ensure that the donated blood cannot be shipped from a mobile blood facility to a main center which is not assigned to it. The same applies to constraints (4.20) considering permanent facilities and main centers. Considering the example depicted in figure 4.3 and $t = 1$, at the collection point MF2, it is not possible to collect blood from DG1 because the donors from DG1 are not assigned to MF2 but to MF1. Both MF1 and MF2 are

assigned to MC, so all blood collected at both facilities can be shipped to MC.

$$Q_{ijt} \leq vX_{ijt}, \quad \forall i, j, t \tag{4.17}$$
$$Q_{ilt} \leq vX_{ilt}, \quad \forall i, l, t \tag{4.18}$$
$$Q_{jkt} \leq vX_{jkt}, \quad \forall j, k, t \tag{4.19}$$
$$Q_{lkt} \leq vX_{lkt}, \quad \forall l, k, t \tag{4.20}$$

Constraints (4.21) assure that every group of donors, in each period, can only donate blood to either a mobile blood facility or a permanent facility, but not to both. Also, it guarantees that every group of donors only donate blood to a single location, i.e., a group of donors can not donate blood in two permanent facilities nor two mobile blood facilities. In the presented example (figure 4.3), DG2 can only donate blood at MF1 or MF2, in the same period, but not at both.

$$\sum_{j} X_{ijt} + \sum_{l} X_{ilt} \leq 1, \quad \forall i, t \tag{4.21}$$

Constraints (4.22) and (4.23) guarantee that in each period each blood collection facility, either mobile or permanent, respectively, is not assigned to more than one main center. Moreover, blood can only be delivered from a mobile blood facility from where it is located, which is guaranteed by constraints (4.24).

$$\sum_{k} X_{jkt} \leq 1, \quad \forall j, t \tag{4.22}$$
$$\sum_{k} X_{lkt} \leq 1, \quad \forall l, t \tag{4.23}$$
$$X_{jkt} \leq Z_{jt}, \quad \forall j, k, t \tag{4.24}$$

Constraints (4.25) assure that in each period the total demand should be satisfied.

$$\sum_{j,k} Q_{jkt} + \sum_{l,k} Q_{lkt} \geq D_t, \quad \forall t \tag{4.25}$$

Constraints (4.26) and (4.27) define the domains of the decision variables.

$$Y_{j_1,j_2,t}, Z_{lt}, X_{ijt}, X_{ilt}, X_{jkt}, X_{lkt} \in \{0, 1\}, \quad \forall i, j, k, t \tag{4.26}$$
$$Q_{ijt}, Q_{ilt}, Q_{jkt}, Q_{lkt} \geq 0, \quad \forall i, j, k, t \tag{4.27}$$

The model built by equations (4.1) to (4.27) is of type Mixed Integer Programming (MIP) and models a generic blood collection planning problem with a set of donor groups, collection points, both permanent and mobile, and main centers, with the goal of minimizing the total BSC costs. All collected blood at collection points must be shipped to the main centers to ensure all demand is satisfied. This MIP model is referred to as the core model in the following chapters.

Based on the data made available by the IPST, it was necessary to include new concepts in the proposed model so that it better represents the Portuguese BSC. These new concepts will be discussed in the following section.

4.4 Additional Constraints Applicable to the Available IPST Data

For the model built by equations (4.1) to (4.27) presented in the previous section to better model the Portuguese scenario, new concepts had to be introduced along with their respective model parameters. They are the maximum daily number of collected blood pack units, *M*, and a maximum number of allowed mobile blood facilities that can be moved in each period, *N* and *N'*. Consequently, new constraints had to be added to the MIP base model presented in the previous section, which will be detailed below. In Chapter 5, the need for adding these constraints is demonstrated.

To try to minimize the number of blood units that are wasted, a limit has been imposed on the number of blood pack units that can be collected per day. Constraints (4.28) ensure that the number of blood pack units collected in each period does not exceed the maximum allowed value. For example, considering $M = 50$ units, between donor groups DG1 and DG2, and collection points MF1 and MF2, it is not possible to collect more than 50 units of blood on the same day.

$$\sum_{i,j} Q_{ijt} + \sum_{i,l} Q_{ilt} \leq M, \qquad \forall t \tag{4.28}$$

Constraints (4.29) and (4.30) guarantee that the model does not move more mobile blood collection facilities than the ones that are allowed. Constraints (4.29) are responsible for defining this limit for the weekdays, from Monday to Friday, and constraints (4.30) for the weekend days, Saturday and Sunday. These constraints limit the number of collection sessions that can take place per day so that there are not too many units of blood to be collected that could end up being wasted.

$$\sum_{j_1} \sum_{t'=t-6}^{t-2} Y_{j,j_1,t'} \leq N, \qquad \forall k, j = k, t \geq 7 \tag{4.29}$$

$$\sum_{j_1} \sum_{t'=t-2}^{t} Y_{j,j_1,t'} \leq N', \qquad \forall k, j = k, t \geq 7 \tag{4.30}$$

To guarantee that the blood donations are not always made by the same donor groups, a minimum interval of *d'* days between two consecutive donations of the same donor group has been imposed. Constraints (4.31) ensures this interval. Looking again at the example depicted in figure 4.3 and considering $d' = 30$ days, if the donors from DG2 donated blood on day 1 in MF2, they will have to wait 30 days to be able to donate again, whether in MF1 or MF2, which means DG2 can only give blood again on day 31.

$$\sum_{t'=t}^{t+d'} \sum_{j} X_{ijt'} \leq 1, \qquad \forall i, t \leq |T| - d' \tag{4.31}$$

Constraints (4.32) assure that, in each week, at least ω-percent of the average number of collected blood units should be satisfied. With constraints (4.25), there is a need for demand values, but these data were not available. So, constraints (4.32) replace constraints (4.25) of the base model.

$$\sum_{t'=t-6}^{t} \left[\sum_{j} Q_{jkt'} + \sum_{l} Q_{lkt'} \right] \geq \omega A_{kw}, \qquad \forall k, t\%7 = 0, w \tag{4.32}$$

With these additional constraints (4.28)-(4.32), the following model is built:

$$(4.1) - (4.24)$$

(4.26) − (4.32)

This new model is referred to as the model considering all constraints in the following chapters and models a generic blood collection planning problem adapted to the reality of the Portuguese BSC.

4.5 Additional Constraints not Applicable to the Available IPST Data

This section presents some constraints and the respective parameters and decision variables that could be added to the core model presented above, enriching it and allowing it to cover more aspects/echelons of the BSC. The following constraints were not considered for evaluation purposes in this thesis because there was no available data to test and validate them.

From the BSC echelons not considered in the developed model, the one that would have a more direct impact on the model's results would be the distribution stage. By including this level, hospitals will be considered in the model, and actual consumption values could be used to test and validate the model. The distribution echelon is considered in this new model by adding the demand points layer in the previous network, thus allowing the transport of blood units from main centers to demand zones. Inventory holding costs are also considered in this new model so that the total costs are as close as possible to reality.

The supply chain network would then comprise blood donor zones, permanent and mobile blood collection facilities, main blood centers, and demand zones. This new model will be more complete when compared with the core model presented above as it will describe the entire flow of blood in the supply chain from the producers, who are the donors, to the end-users, who are at hospitals, passing through the main centers.

The additional notation considering what was described before is described as follows:

Sets	
H	set of demand zones $(h = 1, ..., H)$

Parameters	
c_{kh}	transportation cost per unit of blood between the main center located at k and the demand point located at h
ic_k	inventory holding cost of blood units in main center located at k
ic_h	inventory holding cost of blood units in demand point located at h
v_h	maximum inventory capacity in demand point located at h
d_{ht}	total demand of demand point located at h in period t

Decision Variables	
X_{kht}	a binary variable equal to 1 if a main blood center located at k is assigned to a demand point at h in period t, and 0 otherwise
Q_{kht}	the blood volume (in blood pack units) transported from a main center located at k to a demand point located at h in period t
I_{kt}	the amount of inventory level of blood units in main center located at k in period t
I_{ht}	the amount of inventory level of blood units in demand point located at h in period t

The objective function (4.33) minimizes the total cost of moving mobile blood facilities in each period, the cost of delivering blood from mobile blood facilities and permanent facilities to main blood centers during the planning horizon and between the latter and demand points, and the inventory holding costs in

main centers and demand points.

$$\min \quad \sum_{j_1,j_2,t} c_{j_1,j_2} Y_{j_1,j_2,t} + \sum_{j,k,t} c_{jk} Q_{jkt} + \sum_{l,k,t} c_{lk} Q_{lkt} + \sum_{k,h,t} c_{kh} Q_{kht} + \sum_{k,t} ic_k I_{kt} + \sum_{h,t} ic_h I_{ht} \tag{4.33}$$

Constraints (4.34) ensure that blood can not be transported from the main center to a demand point that is not assigned to it.

$$Q_{kht} \leq v X_{kht}, \quad \forall k, h, t \tag{4.34}$$

Constraints (4.35) and (4.36) denote the inventory capacity of main centers and demand points in each period, respectively.

$$I_{kt} \leq v_k, \quad \forall k, t \tag{4.35}$$

$$I_{ht} \leq v_h, \quad \forall h, t \tag{4.36}$$

Constraints (4.37) assure that a sufficient amount of blood is transported to demand points to meet all demands without facing any shortage.

$$\sum_k Q_{kht} \geq D_{ht}, \quad \forall h, t \tag{4.37}$$

Constraints (4.38) and (4.39) define the domains of the decision variables.

$$X_{kht} \in \{0, 1\}, \quad \forall k, h, t \tag{4.38}$$

$$Q_{kht}, I_{kt}, I_{ht} \geq 0, \quad \forall k, h, t \tag{4.39}$$

The model built by equations (4.2) to (4.27) and (4.33) to (4.39) models a generic blood collection planning problem, comprising a network with a set of donors, collection points, main centers, and demand points, where all collected blood is shipped from the collection points to the main centers and from the latter to the demand points, satisfying all hospitals needs.

4.6 Summary

In this chapter, the data provided by IPST, which will be used to validate and test the model, is described, allowing a better understanding of the Portuguese BSC. The problem in question is defined in more detail, and a mathematical formulation is presented, including a description of the model's constraints. Some additional constraints are also included in this chapter to turn the model more generic. These constraints allow the model to be applied to any other scenario than the Portuguese. Moreover, these constraints could have been used in the developed model that describes the Portuguese BSC if more data were available in Portugal.

In the following chapter, the applicability of the developed model to the provided data is demonstrated.

Chapter 5

Experimental Evaluation

In this chapter, the results of the application of the above-explained model to the data provided by IPST are displayed. First, the data used and the assumptions considered are discussed. Then, the description and discussion of the obtained results for the models described in chapter 4 are presented. Finally, the general conclusions of this chapter are carried out.

5.1 Data Treatment and Assumptions

To evaluate the applicability of the model described in Chapter 4, real data from IPST was used. This section explains the data treatment for the data used and the assumptions adopted in the problem under study.

5.1.1 Donors

The donor groups are allocated based on the number of counties in Portugal, totaling 229 donor groups. The capacity of donor groups, v_i, is measured in the number of donors. It is assumed that 20.06% of the population at a national level donate blood, based on the annual report of the Portuguese haemovigilance system corresponding to the year 2019 [6]. In practice, this percentage may differ across regions, but in this thesis, it is assumed it is uniform throughout the country because there was no possibility of explicitly calculating a different percentage for each country region.

5.1.2 Costs

In this thesis, two types of costs are considered: transportation costs and moving costs.

Transportation costs are considered between the collection points and the main centers and represent the cost of transporting blood pack units. The cost per unit of blood was set at 0,14€/km based on values for refrigerated biological transport available in Rupprecht and Nagarajan [79]. This value was multiplied by the distance between the collection points and the main center to obtain the total transportation cost, c_{jk} and c_{lk}, respectively from mobile and permanent facilities.

Moving costs represent the cost of moving the mobile blood facilities from one location to another. It was not possible to obtain information on these costs, as these are not formally quantified by the main centers. Thus, an attempt was made to assign a reasonable value to these costs. As mentioned above, there are two types of mobile blood facilities, those that move vans and medical personnel, and those that only move medical personnel. The cost was set at 0.15€/km for the facilities that include the movement of vans, and 0.05€/km for those that only move personnel. This value was multiplied by the

distance between the two locations to obtain the total moving cost, $c_{j1,j2}$. These costs may not be the most adequate to the reality of Portugal and will not reflect the actual amount spent by the main centers. However, it allows obtaining credible results.

5.1.3 Time

Regarding the time flow, a planning horizon of six months is considered for the CSTL, which is divided evenly and uniformly into 1-day periods, which is equivalent to 180 periods. For the CSTP and CSTC, a time horizon of four months is adopted, which corresponds to 120 periods. The decision to choose this period lies primarily with performance issues. Additionally, it was presumed that this time horizon was sufficiently representative of the behavior of the BSC.

The data corresponding to the year 2019 will be used to demonstrate the validity of the model considering the adopted time horizons.

5.1.4 Considered problem size

Each of the three main centers - CSTL, CSTP, and CSTC - covers a specific area of Portugal, as can be seen in figure 2.1. The available data is divided by CST since there is no interaction between CSTs during the collection process, and each CST collects on its designated area. The problem is therefore split into three distinct sub-problems with the following sizes (see table 5.1).

Table 5.1: Size of the considered problem.

Main Centers	Donor groups	Mobile units	Mobile locations	Permanent facilities	Time periods	Collected blood units
CSTL	52	509	71	4	180	7000
CSTP	68	367	82	1	120	5000
CSTC	109	360	95	1	120	3500

5.2 Results

The model was implemented in OPL programming language and solved by CPLEX (version 20.1.0) on a server with Intel Xeon Silver 4110 CPU, 2,10 GHz and 64 GB of RAM.

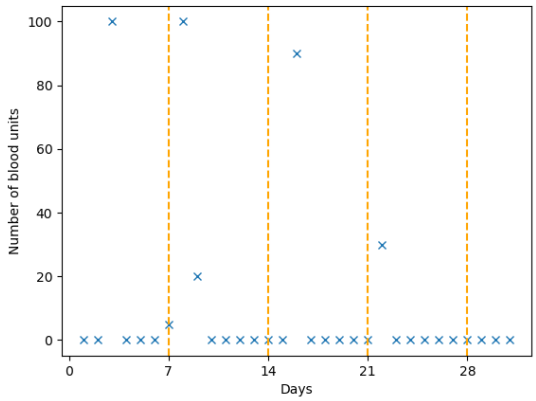
To prove the validity of the core model, daily demand data is required. However, information regarding blood consumption in hospitals was not available as hospitals and main centers do not keep detailed records of this information. So, in order to obtain reliable and realistic results, and considering that the focus of this work is the collection echelon of the BSC, constraints (4.25) of the core model that considered daily consumption values were replaced by constraints (4.32) that take into account the number of units of blood collected per week.

Through the available data, more precisely 2019 data, it was possible to calculate the average number of donated blood units. To guarantee that the model is accurate, the average was calculated separately for each of the main centers. It was also calculated per week, considering that a week is a period of seven days. Table 5.2 shows the obtained value for each main center. Thus, the model tries to collect at least ω-percent of the blood units collected per week in 2019 instead of trying to fulfill the blood demands, which is expressed by constraints (4.32).

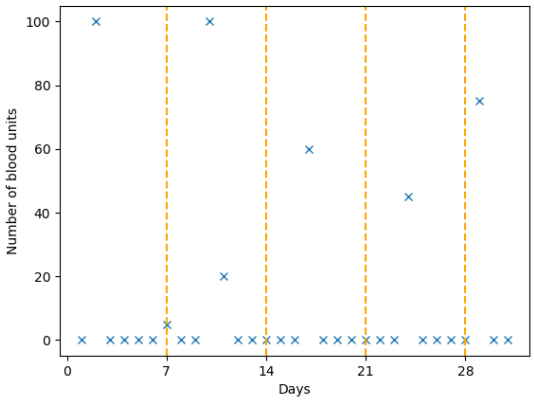
The model was run, and it was noticed that it is executable, and with the considered assumptions up until this point it returned a feasible solution.

Table 5.2: Average number of collected blood pack units per CST per week in 2019.

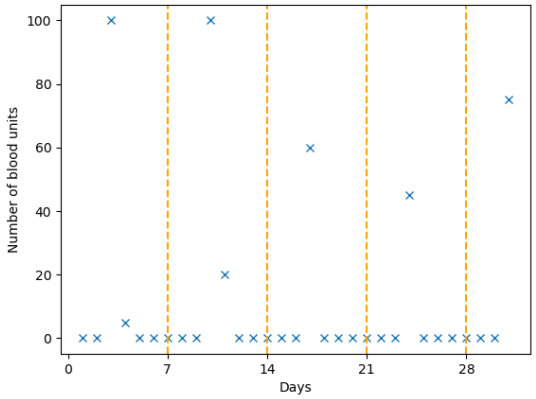
	CSTL	CSTP	CSTC
Average number of collected blood pack units	1400	1670	1140



(a) CSTL



(b) CSTP



(c) CSTC

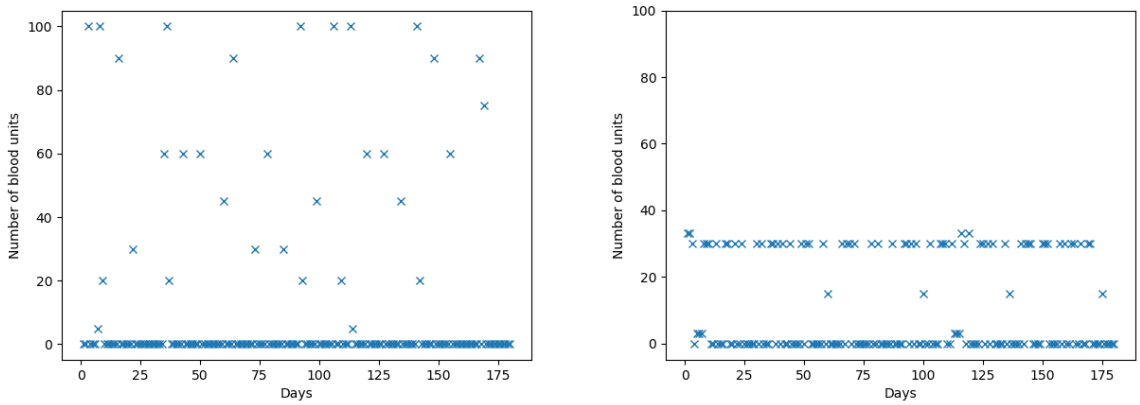
Figure 5.1: Number of blood pack units collected per week for each main center.

5.2.1 Wastage

One aspect that may be analyzed is the wastage of blood since one of the main goals of the BSC is to ensure that there is no shortage of blood units while trying to keep the number of units wasted to a minimum.

When analyzing the model's solution, it was noticed that there were days when too many units of blood were collected and others when no units were collected, with no uniform distribution of blood units collected over the days. There were even weeks in which the average number of blood units equivalent to a week was collected in a single day. Figure 5.1 illustrates this behavior for each of the three main centers, figure 5.1a for the CSTL, figure 5.1b for the CSTP, and figure 5.1c for the CSTC. Here, each vertical line represents the end of a week and each cross represents the number of blood pack units collected each day for a period of one month and considering a $\omega = 0.3$. The model took about 20 minutes to run for each CST to obtain the results displayed in figure 5.1.

In figure 5.1a, it can be seen that in the third week, between the 14th and the 21st, there were only



(a) Before maximum daily limit

(b) After maximum daily limit

Figure 5.2: Number of blood pack units collected per day for the CSTL.

blood collections in one day, as only one day has a non-zero number of collected blood units. This means that the total number of blood units that should be collected in the third week for the CSTL was collected in just one day. The same happened in the fourth week. For the CSTP, the same occurred. It can be seen in figure 5.1b that, in the third and fourth weeks, there were only blood collections in one day each week. In figure 5.1c, the same is verified for the CSTC, with the third and fourth weeks showing the same results.

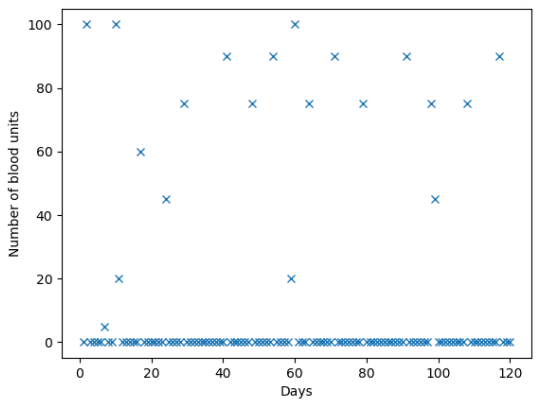
Due to the perishable nature of blood and the fact that blood consumption does not always keep up with donation levels, collecting too many units of blood at once can lead to its waste. To try to prevent the wastage of blood units, it was imposed a maximum number of blood pack units that can be collected per day, forcing the model to not collect more units than the maximum allowed. Based on the available data for 2019, it was possible to calculate the average number of blood pack units collected per day, allowing the attribution of a reasonable value to the maximum number of blood pack units collected per day. That value was set to 200 units of blood for the CSTL, 230 for CSTP, and 160 for CSTC. Constraints (4.28) enforce this limit.

Figure 5.2 shows the number of blood pack units collected per day for a period of 180 days for the CSTL before and after adding constraints (4.28) that impose the maximum daily limit, respectively figure 5.2a and figure 5.2b. In figure 5.2a, it can be seen that the number of collected blood pack units is not uniform among days with some days having a much higher number of collected units than others. After adding the constraints (4.28), the collection of blood units is more distributed among days, as shown by figure 5.2b.

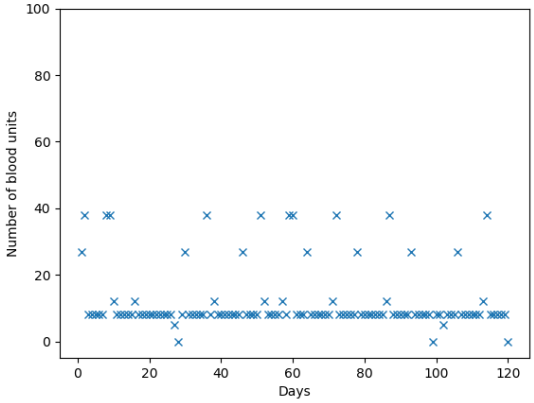
When comparing figures 5.2a and 5.2b, it can be seen that, in figure 5.2b, there are more days when units of blood are collected, as there are more points on the graphic with non-zero values, and these are collected in smaller amounts each day than in figure 5.2a. Collecting a smaller number of units each day prevents the wastage of blood since each blood pack unit after being collected has a limited period during which it can be used and after which it should be discarded.

By analyzing the number of collected blood units, it is visible that this number is much smaller than the established maximum daily limit. This happened because, for computational reasons, the total number of blood units that must be collected per week is lower than the averages calculated and presented above in table 5.2. So consequently, the number of blood units collected per day will also be smaller than the calculated number.

Although each main center is considered as an independent problem, the results obtained for each

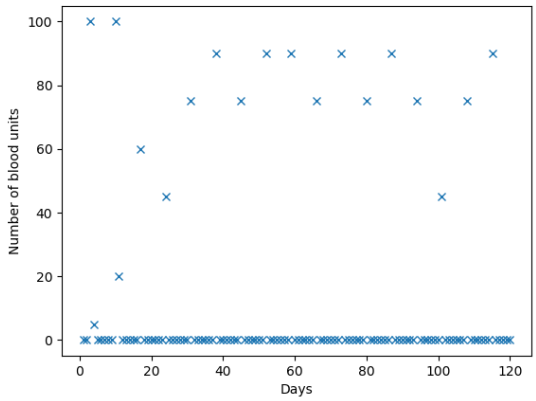


(a) Before maximum daily limit

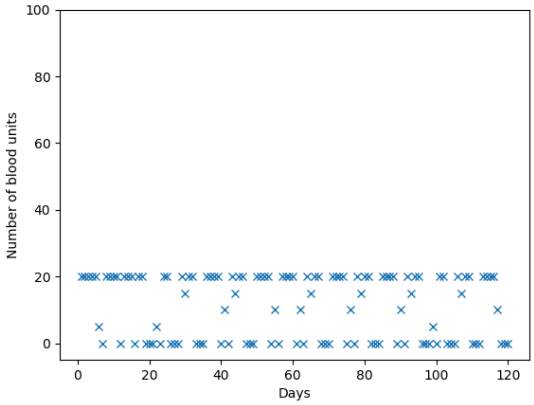


(b) After maximum daily limit

Figure 5.3: Number of blood pack units collected per day for the CSTP.



(a) Before maximum daily limit



(b) After maximum daily limit

Figure 5.4: Number of blood pack units collected per day for the CSTC.

main center are similar to each other, and what was described above for the CSTL is also true for the CSTP and the CSTC. Figures 5.3 and 5.4 show the number of blood pack units collected per day, respectively, for the CSTP and the CSTC, before and after adding constraints (4.28) that imposes the maximum daily limit.

In figure 5.3a, it can be seen that, in the majority of the days, there was no collection of blood units as, in the graphic, there are too many points with a zero value of collected blood units. On the other hand, after adding constraints (4.28), figure 5.3b demonstrates that practically every day, there were collections of blood units, as most of the points on the graphic have a non-zero value of collected blood units.

The same was verified for the CSTC. Figure 5.4a shows an irregular distribution of the number of collected blood units among days with no blood units collected on most days. However, after the addition of constraints (4.28) that imposes the maximum daily limit, there was a more uniform distribution of the number of blood units collected, as shown in figure 5.4b.

In addition to the maximum daily number of collected blood pack units imposed, another way to try to prevent the wastage of blood units is to limit the number of mobile blood facilities that can be moved to collection points in each period. Adding this limit is a way of preventing having too many collection sessions on the same day, and consequently, avoiding collecting too many units of blood at once, which can end up wasted.

Controlling the number of mobile blood facilities that can be moved is also a measure of controlling the number of professionals needed in each collection session. For each blood collection session, it is necessary to move a multidisciplinary team from the CST associated to that collection point to carry out the collection. So, by limiting the number of collection sessions, it is possible to ensure that the limited number of human resources is not exceeded, making the model more reliable.

Through the available data, it was possible to calculate the average number of collection sessions made in 2019 for each CST. As the number of collection sessions is different for the weekdays and the weekend days, two constraints were added to the model to assure it is trustworthy, constraints (4.29) and (4.30). Constraints (4.29) ensure that the model does not move more mobile blood collection facilities than those that are allowed for weekdays. Constraints (4.30) guarantee the same for the weekend days.

The addition of the limits discussed above aims to ensure that the number of wasted blood units is as minimal as possible, as the model tries not to collect units in excess. These limits can also be used to control the number of blood units that can be processed daily by the main centers, ensuring that all collected blood units can be processed and stored for later use.

Now that the blood wastage has been discussed, it is necessary to look at the geographic dispersion of the blood collection sessions by analyzing the locations chosen by the model for the collection points. This analysis is done in the following section.

5.2.2 Geographic dispersion

By analyzing the solution obtained for each main center about the locations chosen by the model after adding the constraints mentioned above, it was noticed that the blood collections always took place in the same municipalities, particularly in those located closer to the main center. This happened mainly due to the following factors: (1) the model prefers locations that are at a shorter distance from the main center since the transportation costs are lower once these are obtained through the distance between the main center and the collection points, which is in line with the goal of cost minimization; (2) as donors are considered by groups and not individually, no restriction prevented the same donor group from donating blood whenever collections were organized in a specific county, even if the collections were on consecutive days.

Firstly, will be analyzed the results for the CSTL, then for the CSTP, and finally for the CSTC.

Figure 5.5 shows the geographic distribution of CSTL collection points after running the core model with the constraints discussed above. Each orange point represents a municipality where blood collections took place. If there was more than one blood collection session in the same county, which is possible because there is more than one blood collection unit per county, there is only one orange point in the figure. The green point represents the main center, in this case, the CSTL, and the blue arrow describes the assignment between the collection point and the main center.

Looking again at figure 5.5, it can be seen there is no considerable geographic dispersion, as all blood collection sessions were carried out in neighboring locations, which is not faithful to reality as blood donations occur in different places across the country. Despite existing a restriction that guarantees that there is a minimum interval of d days between collections, what happens is that, in each county, there are different mobile blood collection units, and each one has an identification number associated, being this restriction applied to each identifier and not the county itself. Thus the model always selects units from the closest counties once they are at a shorter distance from the main center.

To force the geographic dispersion of collection points, constraints (4.31) have been added to the model. These constraints impose a minimum day interval between donations from the same donor group enforcing the model to choose different locations to reach its goals since the donor groups are allocated based on the Portuguese counties. With the addition of these constraints, the model becomes more

Figure 5.5: The result of the core model for launching collection facilities for the CSTL.

Figure 5.6: The result of the model for launching collection facilities for the CSTL after adding constraints (4.31).

realistic since there is a time interval of 2 months between donations imposed by the Portuguese law. As the donors are distributed by groups, it was considered that the interval between donations of the same donor group was of 2 weeks.

Figure 5.6 shows the geographic dispersion of CSTL collection points after running the model with constraints (4.31). It can be seen that now, with the imposed time interval between donations of the same donor group, the model has to choose locations that are at a longer distance from the main center because it is forced to choose more locations to achieve its goals since each donor group donates less often. Consequently, the model has higher costs as it has to move more mobile collection units and move them to locations further away, but the truth is that these constraints are needed because they make the model more realistic and trustworthy.

Considering now the CSTP results', figures 5.7 and 5.8 show, respectively, the locations that have been chosen by the model for launching collection units for the CSTP before and after adding constraints (4.31).

Comparing figures 5.7 and 5.8, it can be seen that with the addition of the time interval between donations from the same donor group, imposed by constraints (4.31), there is an increase in the number

Figure 5.7: The result of the core model for launching collection facilities for the CSTP.

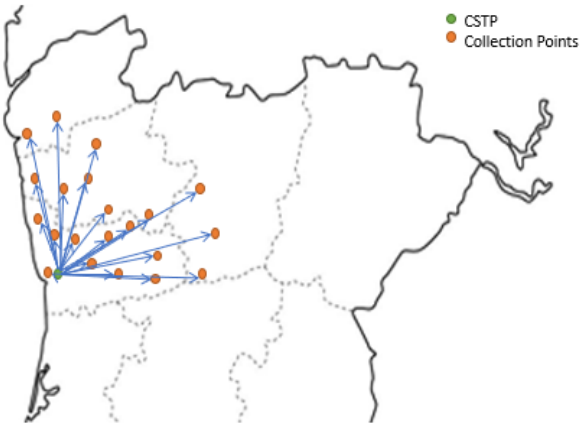


Figure 5.8: The result of the core model for launching collection facilities for the CSTP after adding constraints.

of counties where blood collections take place, which consequently increases the number of collection units used, as previously described for the CSTL. This increase is because each donor group has a period during which it cannot donate blood, so to achieve the model's goals, there is a need to organize more collection sessions.

Analyzing the results for the CSTC, figures 5.9 and 5.10 illustrate the geographic distribution of CSTC collection points before and after adding constraints (4.31), respectively.

Comparing figures 5.9 and 5.10, referring to the CSTC, with the ones presented before for the CSTL and the CSTP, it can be seen the results are similar for all main centers. Before adding constraints (4.31), there is no considerable geographic dispersion of the locations chosen for the blood collections, ending up always being the same donor groups to make the donations. After adding these constraints, all main centers are forced to move more mobile units to ensure that the desired number of collected blood units is achieved, requiring different donor groups to donate.

The similarity between solutions obtained for the CSTL, the CSTP, and the CSTC demonstrates how the model is generic and can be applied to any main center regardless of its geographic location and the area it covers.

The addition of the constraints discussed above aims to ensure the model's reliability while giving the possibility for all donor groups to donate blood easily, as donors do not have to travel large distances to donate blood once the model forces the movement of mobile units to different locations.

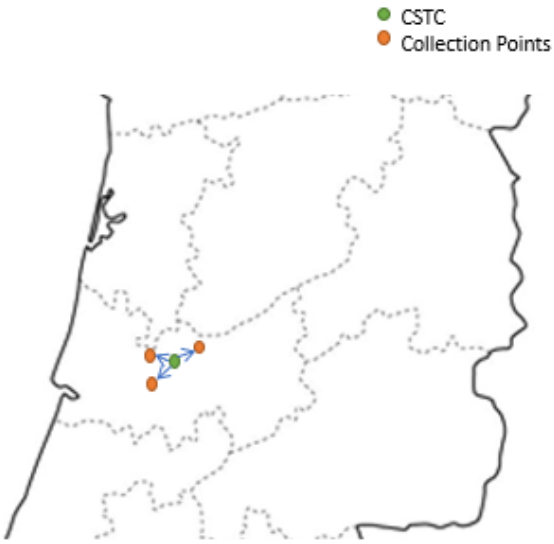


Figure 5.9: The result of the core model for launching collection facilities for the CSTC.

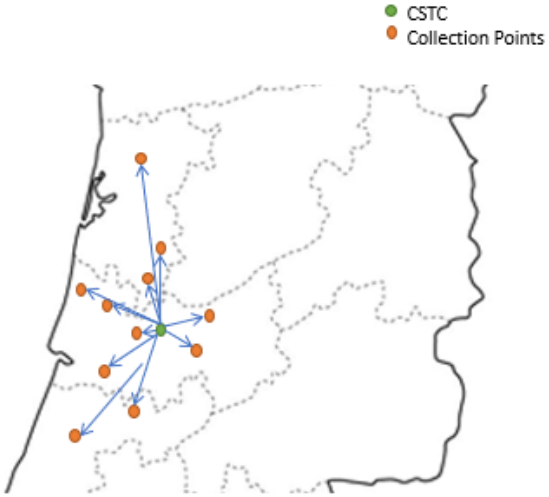


Figure 5.10: The result of the core model for launching collection facilities for the CSTC after adding constraints.

Now that the geographic dispersion of collection points has been discussed, it is necessary to analyze the allocation of donor groups to the collection facilities, which will be done in the following section.

5.2.3 Allocation

To establish the allocation of donor groups to blood facilities, both mobile and permanent, it was considered the distance (in kilometers) between the donor groups and the collection points. As before, these allocations between the donor groups and the collection points will be analyzed separately for each of the main centers, starting with the CSTL, then the CSTP, and finally, the CSTC.

The allocation of donor groups from the Lisbon metropolitan area to CSTL collection points is depicted in figure 5.11. Here, each orange point represents a donor group, each green point represents a mobile blood collection facility, and each yellow point represents a permanent collection unit. The blue arrows indicate that a donor group is allocated to a collection point. All the donated blood is then shipped from

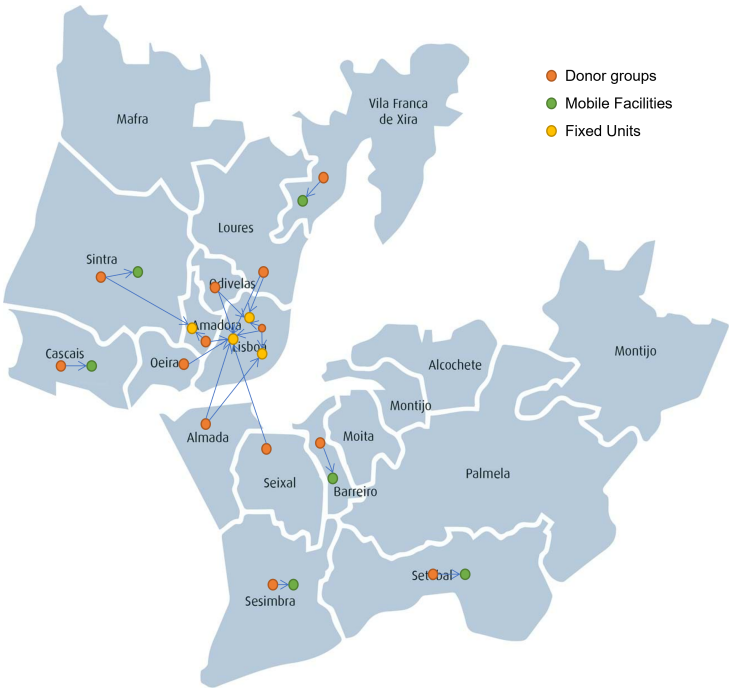


Figure 5.11: Allocation of CSTL blood donor groups to blood facilities.

the collection points to the main centers.

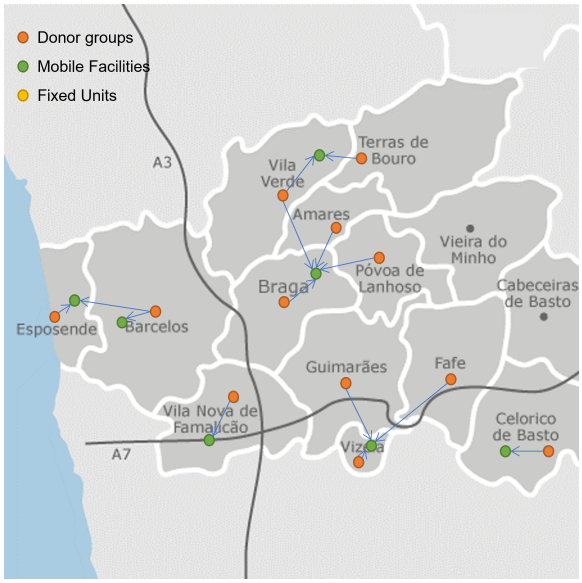
As can be seen in figure 5.11, not all counties have an orange point which means that the model never allocates the donor groups from those counties to any collection facility. In addition and considering the area covered by the CSTL, the model never moves mobile units to the Algarve and Alentejo regions, which represent the country regions' with the lowest donation rate in 2019. These results mean that the model can achieve its goals without needing the donor groups from those regions. This model's behavior can be explained by its goal of cost minimization since the higher the number of mobile units moved, the higher the costs. It can also be justified by the reduced interval between donations of the same donor group that is being considered.

Looking again at figure 5.11, it can be noticed that the donor groups are assigned to the nearest facilities, which is in line with the donors' goal of walking or driving shorter distances, as studied by Ramezanian and Behboodi [61]. When analyzing the locations chosen by the model, it is visible the model's preference to move mobile units to furthest away locations, despite increasing costs, as the donor groups closer to the permanent points donate there. That can be seen in figure 5.11 as the donor groups that are closer to the fixed points are allocated to them. This allocation is coherent with the model's goal of cost minimization since permanent facilities have lower costs than mobile units. The costs are lower because there is no need to move vans or multidisciplinary teams to the collection points, and the distance between the fixed points and the CSTL is smaller than for most mobile units. So, the donor groups closer to permanent facilities donate there not being necessary to move mobile units to those places.

Considering now the donor groups in the area covered by the CSTP, figure 5.12 shows the allocation of these donor groups to the blood collection facilities. The figure separately presents the allocation of the donor groups for each CSTP district to be more readable. Figure 5.12a is related to Porto's district, figure 5.12b to Braga, figure 5.12c to Viana do Castelo, and figure 5.12d to Vila Real.

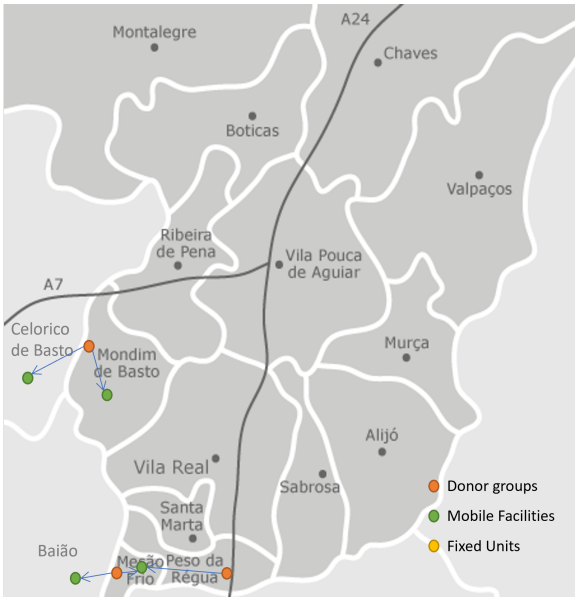
Figure 5.12 shows that the donor groups are allocated to the nearest facilities. As before, the results obtained for the CSTP are similar to those obtained for the CSTL, demonstrating an evenly model's behavior.

(a) Allocation of Porto blood donor groups to blood facilities



(b) Allocation of Braga blood donor groups to blood facilities

(c) Allocation of Viana do Castelo blood donor groups to blood facilities



(d) Allocation of Vila Real blood donor groups to blood facilities

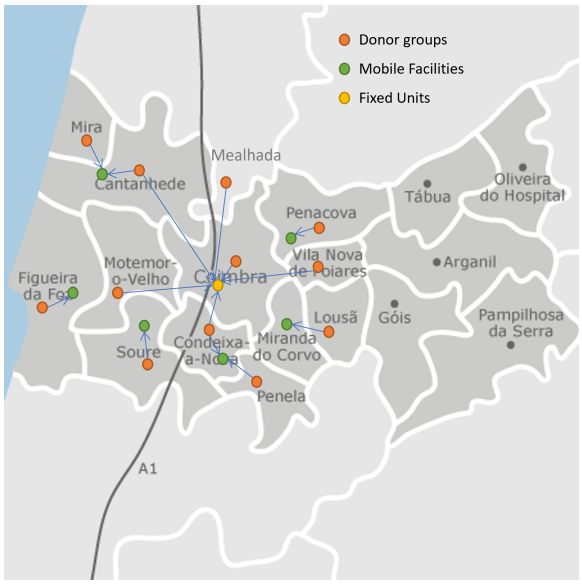
Figure 5.12: Allocation of CSTP blood donor groups to blood facilities.

Looking again at figure 5.12, it can be seen that Porto and Braga regions', respectively figures 5.12a and 5.12b, are the regions where there are more blood collection sessions since those are the places where there are more collection points. This behavior is consistent with the fact that these are the most densely populated regions in the area covered by the CSTP, and therefore with the most donors.

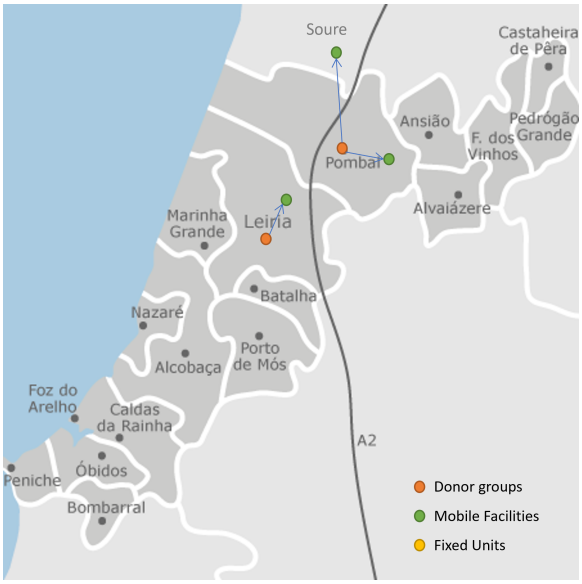
Figure 5.13 displays the results of the allocation of CSTC donor groups to the blood collection facilities. As expected, the results presented in figure 5.13 for the CSTC are identical to those discussed above for the CSTL and the CSTP.

By analyzing figures 5.12 and 5.13 referring to the CSTP and the CSTC, respectively, and considering the designated area of each main center, it can be seen that not all counties have an orange point, which means the model can achieve its goals without needing all donor groups from the areas covered by the

(a) Allocation of Aveiro blood donor groups to blood facilities



(b) Allocation of Coimbra blood donor groups to blood facilities



(c) Allocation of Leiria blood donor groups to blood facilities

Figure 5.13: Allocation of CSTC blood donor groups to blood facilities.

CSTP and the CSTC. Once again, this behavior can be justified by the model's goal of cost minimization since the higher the number of mobile units moved, the higher the costs, and the reduced interval between donations of the same donor group that is being considered.

Despite all considered and previously analyzed constraints, there are always more distant locations where the model never moves mobile units, which consequently means that there are donor groups that are never allocated to any collection point, not making blood donations. This behavior is justified by the model's goal of costs minimization, and the further the collection point, the higher the cost. So, the model tries to organize the blood collection sessions as close as possible to the main centers to ensure lower costs, giving preference to fixed collection points.

Now that the model has been discussed about the obtained results, it is time to analyze the model

concerning time consumption and costs, which will be done in the following section.

5.2.4 Time and cost analysis

The time consumed by the model to find a solution and its costs are discussed below.

Figures 5.14 and 5.15 show the relationship between the time model took to find a solution for each main center and its cost. Figure 5.14 concerns the core model, while figure 5.15 considers the model with all constraints presented in the previous chapter. In both figures, each line represents one main center, and each cross represents the normalized cost of a solution found, with the optimal solution identified by a yellow square.

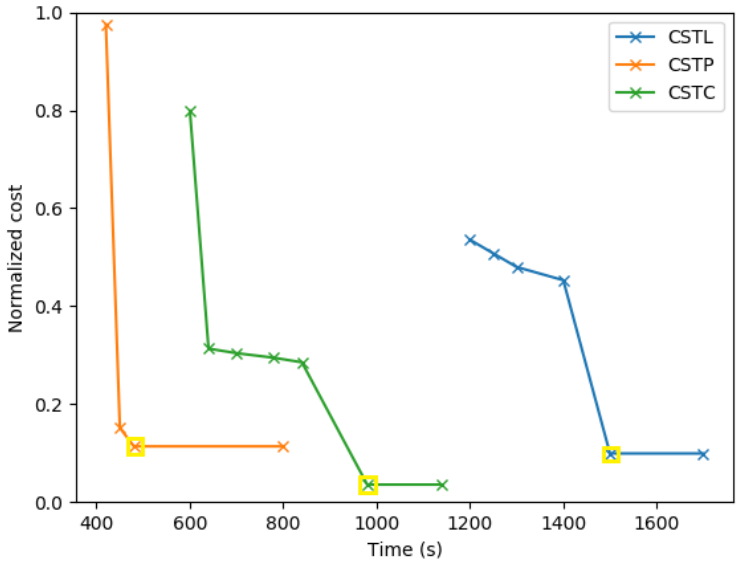


Figure 5.14: Running time and cost of the core model.

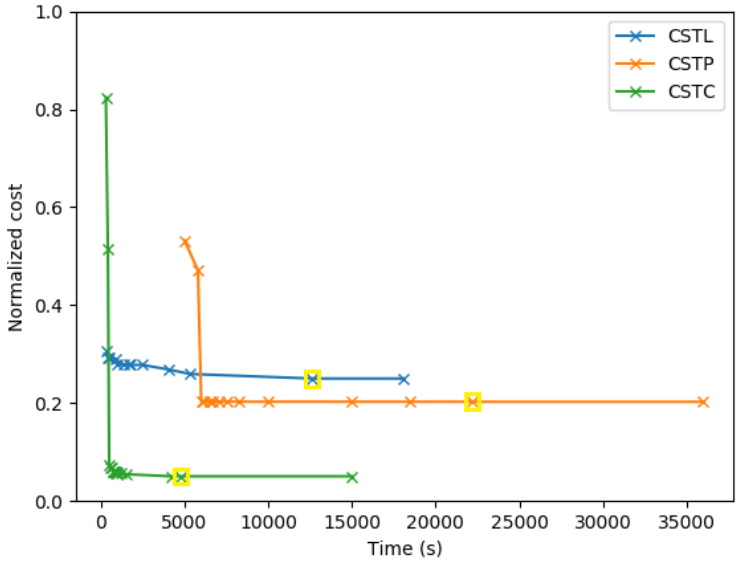


Figure 5.15: Running time and cost of the model with all constraints.

By analyzing figure 5.14, it can be seen that the model finds multiple solutions for each main center, taking more time to find an optimal solution for the CSTL than for the CSTC or CSTP. This difference can be explained by the fact that, for the CSTL, there are more mobile blood facilities than for the CSTC or CSTP. There is, therefore, more choice about where to establish the collections points, which increases the size of the problem, and consequently, increases the time the model takes to find the best places for the collection points.

Moreover, it can be seen that for the CSTP, the model takes more time to prove the solution is optimal than it does to find it once the time interval between finding the optimal solution and terminating is greater than the interval between finding the first solution and the optimal solution. For the CSTL and CSTC, it is the opposite. The model takes more time to find the optimal solution than it does to prove it is optimal.

Looking again at figure 5.14 and comparing the costs of the optimal solution of the three main centers, CSTC has lower costs than CSTL and CSTP because it is the main center that moves fewer mobile blood facilities. This result can be explained as the CSTC is the main center with the lowest average number of collected blood units in 2019, as shown in table 5.2. Regarding the costs of the optimal solutions for the CSTL and CSTP, it can be seen they are similar, meaning that the model's behavior for these two main centers is identical, which makes sense as both Lisboa and Porto are two large urban centers.

The model considering all constraints imposes more boundaries and, consequently, becomes more complex to solve. Thus, when comparing figures 5.14 and 5.15, it can be seen that the model with all constraints, presented in figure 5.15, takes more time to run for all main centers than the core model, showed in figure 5.14, as would be expected.

Contrary to what happened for the core model, now the CSTP is the main center for which the model takes longer to find the optimal solution. The geographical area covered by CSTP is densely populated, and there is only one permanent facility in the region. That can explain the longer time the model takes to find the optimal solution since it prefers to allocate the donor groups to permanent facilities first rather than to mobile units to keep the costs as low as possible.

Regarding the costs of the optimal solution of the three main centers, it can be seen that for the CSTL and CSTP, the cost is higher for the model that considers all constraints, shown in figure 5.15, than for the core model presented in figure 5.14. This higher cost can be justified as to solve the model considering all constraints there is a need to move more mobile blood collection facilities than to solve the core model.

5.2.5 Cost function analysis

In this section, for each main center, namely CSTL, CSTP, and CSTC, a comparison is made between the obtained results and the available data for the year 2019 about the type of collection facilities where most blood donations occurred. Based on the provided data and the obtained results, some statistics were obtained regarding where had been made more donations in the time horizon considered. This analysis is made with the goal of demonstrating the impact of the objective function on the results obtained, whose goal is to minimize the total costs of the BSC.

Firstly, it is analyzed the CSTL. Figure 5.16 compares the available data with the obtained results for the CSTL regarding the type of collection facilities used. In the first six months of 2019, 31 060 blood donations were registered by IPST, of which 18 402 occurred in mobile units, representing 59.34% of the total registered donations and 40.66% in permanent facilities, which is equivalent to 12 657 donations. By analyzing the developed model's solution in figure 5.16, it can be seen that the number of donations both in mobile units and fixed points, respectively 1095 and 2055, is smaller than the number of registered donations by IPST. This difference is justified because, for computational reasons, the considered total number of collected blood units presented in table 5.1 had to be smaller than the total number of donations registered by IPST. Considering the total number of donations with the model, 34.77% occurred in mobile

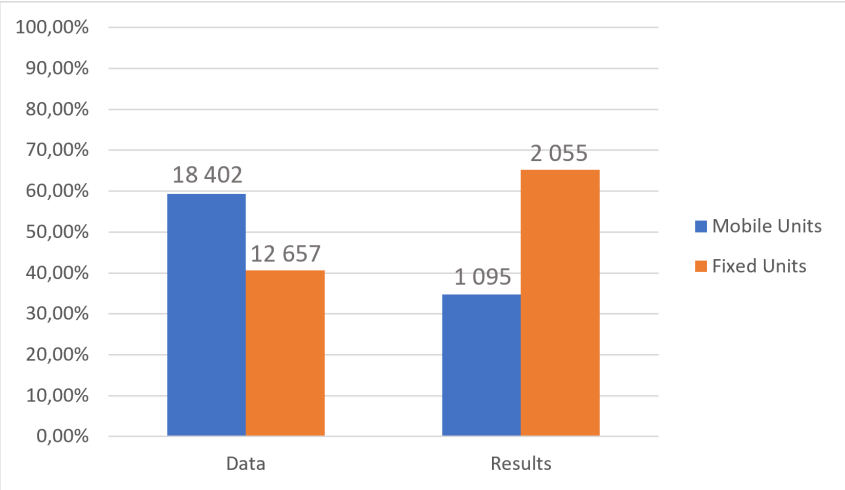


Figure 5.16: Comparison between the data for 2019 and the obtained results for the CSTL.

facilities and 65.23% in permanent points.

When comparing the obtained results with the ones acquired from the data, it can be seen that the results are not similar once, with the model, there are more donations in the fixed points than in mobile units, and with the data, it is the opposite. This behavior is related to the model's goal of cost minimization. To keep the model's costs to a minimum, the model tries to move as few mobile blood collection units as possible, preferring to allocate the donors to permanent facilities rather than mobile units where the costs are higher.

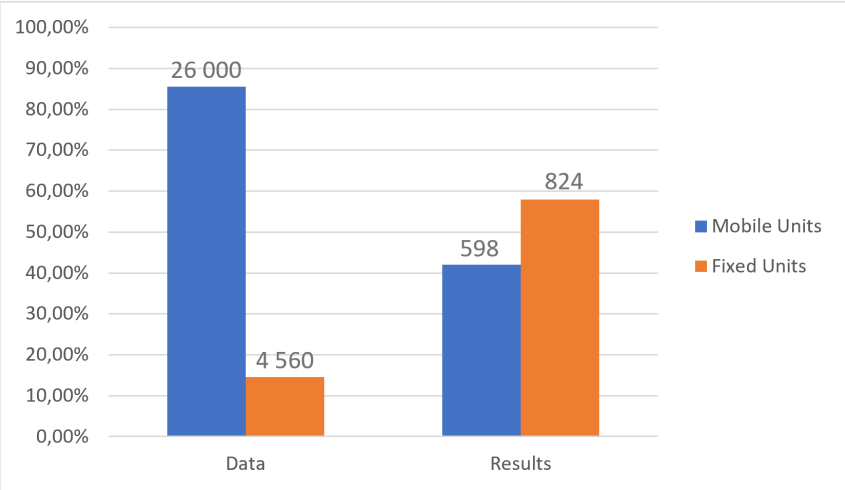


Figure 5.17: Comparison between the data for 2019 and the obtained results for the CSTP.

For the CSTP, it is also visible a difference between the values obtained from the data and the model's results. Figure 5.17 shows this difference. In 2019, in the first four months, 30 560 blood donations were registered by the IPST, of which 85.50% took place in mobile units and only 14.50% in permanent facilities. Considering the model's results, 42.06% of the donations were in mobile units and 57.94% in permanent facilities. Once again, there is a discrepancy between the total number of donations registered by IPST and those obtained by the model that can be justified by computational reasons. However, the CSTP is the main center for which the statistics obtained through the model's solution are closest to each other, meaning the number of blood donations in mobile units and permanent facilities is more identical. This can be explained because the area covered by the CSTP is densely populated, and there is only one

permanent collection facility. So, the model needs to move more mobile blood collection units to achieve its demand goals, being the distribution of donations between mobile and fixed points more similar.

Looking at the results for the CSTC depicted in figure 5.18, it is evident a behavior similar to the ones described before for the CSTL and CSTP, both in relation to the smaller number of blood donations verified with the developed model and to the distribution of the donations between mobile units and fixed units. Once again, it can be seen that in the data from IPST, most of the donations occurred in mobile units, representing 67.32% of the total registered records, with the remaining 32.68% of the donations taking place in permanent points. Concerning the model's results, 28.11% of the donations were in mobile units and 71.89% in permanent facilities, which is explained by the lower costs associated with the permanent facilities comparing to mobile units.

Figure 5.18: Comparison between the data for 2019 and the obtained results for the CSTC.

The demonstrated difference in the results between the IPST data and the developed model can be explained by the model's goal of cost minimization and the shortened time horizon considered. Although the obtained model results are not very close to the IPST data, the truth is that these results can be a relevant indicator for future planning of the blood collection sessions, as they demonstrate that the total BSC costs can be lower when prioritizing blood collections at the existing fixed blood collection points.

5.3 Discussion

The obtained results are analyzed from three distinct points of view. The analysis started with the wastage of blood units, intending to demonstrate that the proposed model tries to hold the number of wasted blood units to a minimum. Then, the geographic dispersion of the collection sessions was analyzed to show that the model tries as much as possible to distribute the collection sessions across the country so that all donors can make donations. Finally, the allocation of donors to the collection points, both fixed and mobile, was discussed, demonstrating that donors prefer to travel or walk to the nearest collection points to cover shorter distances than to further away locations. The analysis according to each of these points was carried out in more detail throughout the previous sections.

The results presented above demonstrate that the developed model prefers the allocation of the donor groups to fixed collection points over mobile units, which is explained by the higher costs associated with the latter. The results also showed that some donor groups have never been allocated to collection points since the model never moves mobile units to locations near those donor groups. This model behavior is because of its goal of cost minimization. The model tries to keep the number of mobile units that are

moved to a minimum.

The choice of considering the donors by groups and not individually lies with computational reasons, as going to the donor level individually would be computationally heavier due to the greater consumption of memory and time. If the focus of this thesis was to study the BSC from the donors' point of view, it would have been more reasonable to consider the donors individually and not by groups. However, the obtained results are sufficiently realistic to justify the absence of the need for detailing at the level of individual donors. The main disadvantage of this choice is related to the time interval between each donor's donations. This interval imposed by the Portuguese law is of 2 months, but as donors were considered by groups, this value had to be relaxed to obtain solutions to the proposed model. The value used for this interval was 2 weeks.

About the time consumption, the model considering all constraints took more time to run when compared with the core model, as would be expected since the core model has fewer constraints, being less complex to solve. The model considering all constraints took about 5 hours to run and return the optimal solution for the CSTL, 9 hours for the CSTP, and 4 hours for the CSTC. Considering the costs, CSTL is the main center with the highest costs, followed by the CSTP, and finally, the CSTC. These differences between the main centers, in terms of time consumption and costs, can be justified by the different characteristics of each region.

In the area covered by the CSTL, the majority of the population is concentrated in the region closest to the CSTL, particularly in Lisbon and Vale do Tejo regions. In the area covered by the CSTP, the population is more geographically dispersed, with high population concentrations in more distant places, such as in the cities of Porto and Braga. Despite these differences, the costs are similar between these main centers. The similarity between the CSTL and CSTP costs can be justified as the regions covered by these centers, Lisboa and Porto, respectively, are large urban centers. The time is not as similar as the costs because there are more fixed collection points in the CSTL region than in the CSTP. Therefore, the model takes longer to allocate the CSTP donors than the CSTL ones. The CSTC has lower costs than the remaining main centers because it is the main center that moves fewer mobile collection units. This behavior is because the area covered by the CSTC is the country region with fewer population and consequently the fewest blood donations.

Finally, a comparison between the obtained results and the data provided by IPST is carried out to analyze where more blood donations occurred, whether in mobile units or fixed points. The results discussed above demonstrated that due to the model's objective function of minimizing costs, most of the model's blood donations took place at fixed points, while in the data made available by IPST, most of the registered donations occurred in mobile units.

From the analysis of the results, it can be concluded that the developed model is reliable and presents realistic results, accurately characterizing the collection echelon of the Portuguese BSC.

5.4 Summary

In this chapter, the results of the application of the proposed model are discussed and analyzed. The data used to apply the model is identified, and the assumptions and the data treatment performed are also covered. The time the developed model took to run is analyzed, along with its cost. Additionally, it is made a comparison between the obtained results and the data provided by IPST. Finally, a brief discussion of the obtained results is provided, highlighting that the model prefers the allocation of donors to fixed collection points rather than mobile blood collection units. Therefore, it is recommended that IPST encourage blood donations at fixed collection points.

Chapter 6

Conclusions and Future Work

Managing a blood supply chain to ensure its efficiency and making a trade-off between blood wastage and shortages is challenging, mainly due to the unique characteristics of blood, such as its perishability and the different blood products' shelf-lives. Indeed, what makes blood a singular and scarce resource is that it can only be produced by human beings, not existing other products to substitute it or chemical processes that can be used to generate blood. Thus, the BSC management depends on donors' voluntary donations, which should be encouraged in the population to ensure there is no shortages. Given this, the optimization of planning blood collections is an evident goal, as the main objective of an efficient BSC is to have the right amount of blood products available where is needed and at the right time.

The main goal of this thesis is to contribute to the efficient management of the BSC by addressing the blood collection problem. There are multiple aspects to take into account in managing the planning of blood collections that depend on the context of each country. Thus, the objective of this work is, firstly, to understand how the Portuguese blood supply chain works and how blood collection management is organized in Portugal. Secondly, this thesis aims to propose a mathematical model for improving the planning of blood collections. To these ends, this work was developed in collaboration with IPST, the entity responsible for managing the Portuguese BSC, to understand the needs and limitations involved in its management, allowing a more precise formulation of the model's constraints.

Considering the analyzed literature, it was concluded that the best approach to address the problem of managing the planning of blood collections was through an optimization model able to help with the definition of optimal locations for establishing blood collection facilities. To do so, the encountered needs and limitations of the BSC were formally defined, allowing the development of an integer programming model that aims to minimize the BSC total costs while determining the optimal location of mobile blood collection facilities. An additional formulation was proposed, considering more aspects of the BSC beyond blood collection, allowing the model to be more general. Due to the current lack of data available, this new formulation was neither tested nor validated in this work, but can be tested once data becomes available.

In the current Portuguese scenario, there are blood transfers between the main centers because some regions are not self-sufficient, meaning they cannot collect what is necessary to satisfy their needs. The truth is that these blood transfers are costly, so in the developed solution, it is assumed that they do not exist, trying to demonstrate whether it is possible or not to satisfy the regions in a self-sufficient way. The obtained results show that it is possible.

The developed model was tested with data provided by IPST, allowing its validation and the obtaining of the model's optimal solution. Using the model also allowed each main center, namely, the CSTL, CSTP, and CSTC, to be studied independently, but on the other hand, it allowed the comparison between them regarding the time the model took to run along with the cost of the optimal solution obtained for each one. This latter analysis showed that the model costs for the CSTL and CSTP are similar, which is explained by

the fact that Lisboa and Porto are two large urban centers. The CSTC has the lowest costs as it collects the fewest units of blood. Additionally, it was possible to compare the solution obtained for each main center with real data from IPST, managing to analyze the behavior of each one.

The analyzes carried out demonstrated that the model can be promising in the future planning of blood collections by pointing out some relevant indicators. An important aspect to take from this study is the room for improvement in the organization of the collection sessions, as the model's results show that costs can be lower when prioritizing blood collections at existing fixed collection points. Another relevant aspect demonstrated by the model's results is that the donors are allocated to the nearest blood collection facilities to walk or drive shorter distances. In fact, these two aspects can be related to each other, and the encouragement of blood donations at fixed collection points through awareness campaigns carried out in local hospitals can be an asset for the IPST. It is therefore recommended that IPST encourage blood donation in local hospitals.

Another recommendation to the IPST would be to consider the possibility of having more fixed collection points spread across the country. Consequently, more donor groups would be able to donate blood easily once there are always more distant places where the model does not move mobile units due to their higher costs. Also, the Portuguese BSC total costs could be lower as it would be necessary to move fewer mobile blood collection units.

The developed approach shows promise in proposing a better blood collection planning for the Portuguese BSC, however, it would require further validation by comparing the results with more accurate data.

6.1 Future Work

The principal limitation of this work is the lack of consumption data. This problem affects both the development and the validation of the model. For example, the distribution echelon was not included in the developed model due to the lack of demand values. Thus, simply acquiring the necessary data could result in an improvement.

Being this one of the first works on the Portuguese BSC, there are a lot of possibilities to continue this study. An interesting analysis would be incorporating blood group types and blood type compatibility at demand zones, which would allow understanding if blood group types were being collected matching demand or not by comparing with accurate values. With this, it would be possible to develop more appropriate blood collection planning strategies, allowing IPST to organize the blood collections according to blood type needs. Additionally, it would also be possible to study the geographic distribution of the population by blood type, allowing a better characterization of the Portuguese BSC. Moreover, the model could be improved to consider uncertainty both in supply and demand, which is extremely important as these parameters are unknown in reality, and this is not addressed in the present work.

This work focuses on the collection echelon of the BSC and the flow of blood between the collection points and the main centers, but many other studies could be conducted related to the BSC. Among them, studies on different specific echelons are a possibility. A study on the distribution stage could be conducted as this is an echelon that handles complex situations and must exist appropriate delivery strategies to ensure the efficiency of the BSC. An in-depth study of the entire BSC, considering all echelons and the whole flow of blood and blood products from donors to patients, is also a possibility.

Bibliography

[1] S. Gunpinar and G. Centeno, "Stochastic integer programming models for reducing wastages and shortages of blood products at hospitals," *Computers and Operations Research*, vol. 54, pp. 129–141, 2015. https://doi.org/10.1016/j.cor.2014.08.017.

[2] S.-M. Hosseini-Motlagh, M. R. G. Samani, and S. Homaei, "Blood supply chain management: robust optimization, disruption risk, and blood group compatibility (a real-life case)," *Journal of Ambient Intelligence and Humanized Computing*, vol. 11, pp. 1085–1104, May 2019. https://doi.org/10.1007/s12652-019-01315-0.

[3] A. Federgruen, G. Prastacos, and P. H. Zipkin, "An allocation and distribution model for perishable products," *Operations Research*, vol. 34, no. 1, pp. 75–82, 1986. https://doi.org/10.1287/opre.34.1.75.

[4] A. F. Osorio, S. C. Brailsford, and H. K. Smith, "A structured review of quantitative models in the blood supply chain: a taxonomic framework for decision-making," *International Journal of Production Research*, vol. 53, pp. 7191–7212, Feb. 2015. https://doi.org/10.1080/00207543.2015.1005766.

[5] J. Beliën and H. Forcé, "Supply chain management of blood products: A literature review," *European Journal of Operational Research*, vol. 217, no. 1, pp. 1–16, 2012. https://doi.org/10.1016/j.ejor.2011.05.026.

[6] IPST,IP, "Plano de atividades," technical report, 2019.

[7] A. M. Araújo, D. Santos, I. Marques, and A. Barbosa-Povoa, "Blood supply chain: a two-stage approach for tactical and operational planning," *OR Spectrum*, vol. 42, pp. 1023–1053, Aug. 2020. https://doi.org/10.1007/s00291-020-00600-1.

[8] K. Katsaliaki and S. C. Brailsford, "Using simulation to improve the blood supply chain," *Journal of the Operational Research Society*, vol. 58, no. 2, pp. 219–227, 2007. https://doi.org/10.1057/palgrave.jors.2602195.

[9] H.-W. Vohr, ed., *Encyclopedic Reference of Immunotoxicology*. Springer-Verlag, 2005. https://doi.org/10.1007/3-540-27806-0.

[10] L. K. Siransy, Z. Y. Nanga, F. S. Zaba, N. Y. Tufa, and S. R. Dasse, "ABO/rh blood groups and risk of HIV infection and hepatitis b among blood donors of abidjan, côte d'ivoire," *European Journal of Microbiology and Immunology*, vol. 5, pp. 205–209, Sept. 2015. https://doi.org/10.1556/1886.2015.00029.

[11] D. D FARHUD and M. Z. Yeganeh, "A brief history of human blood groups," *Iranian journal of public health*, vol. 42, no. 1, p. 1, 2013.

[12] "IPST." http://ipst.pt/index.php/pt/, Accessed: 2021-09-30.

[13] J. T. Blake and M. Hardy, "A generic modelling framework to evaluate network blood management policies: The Canadian Blood Services experience," *Operations Research for Health Care*, vol. 3, no. 3, pp. 116–128, 2014. http://dx.doi.org/10.1016/j.orhc.2014.05.002.

[14] B. Zahiri, S. Torabi, M. Mousazadeh, and S. Mansouri, "Blood collection management: Methodology and application," *Applied Mathematical Modelling*, vol. 39, pp. 7680–7696, Dec. 2015. https://doi.org/10.1016/j.apm.2015.04.028.

[15] H. Min and G. Zhou, "Supply chain modeling: past, present and future," *Computers & Industrial Engineering*, vol. 43, pp. 231–249, July 2002. https://doi.org/10.1016/s0360-8352(02)00066-9.

[16] J. T. Mentzer, W. DeWitt, J. S. Keebler, S. Min, N. W. Nix, C. D. Smith, and Z. G. Zacharia, "DEFINING SUPPLY CHAIN MANAGEMENT," *Journal of Business Logistics*, vol. 22, pp. 1–25, Sept. https://doi.org/10.1002/j.2158-1592.2001.tb00001.x.

[17] B. M. Beamon, "Supply chain design and analysis:," *International Journal of Production Economics*, vol. 55, pp. 281–294, Aug. 1998. https://doi.org/10.1016/s0925-5273(98)00079-6.

[18] M. Christopher, *Logistics & supply chain management*. Pearson Uk, 2016.

[19] M. Melo, S. Nickel, and F. S. da Gama, "Facility location and supply chain management – a review," *European Journal of Operational Research*, vol. 196, pp. 401–412, July 2009. https://doi.org/10.1016/j.ejor.2008.05.007.

[20] M. S. Pishvaee and J. Razmi, "Environmental supply chain network design using multi-objective fuzzy mathematical programming," *Applied Mathematical Modelling*, vol. 36, pp. 3433–3446, Aug. 2012. https://doi.org/10.1016/j.apm.2011.10.007.

[21] B. B. Flynn, B. Huo, and X. Zhao, "The impact of supply chain integration on performance: A contingency and configuration approach," *Journal of Operations Management*, vol. 28, pp. 58–71, June 2009. https://doi.org/10.1016/j.jom.2009.06.001.

[22] M. Cao and Q. Zhang, "Supply chain collaboration: Impact on collaborative advantage and firm performance," *Journal of Operations Management*, vol. 29, pp. 163–180, Dec. 2010. https://doi.org/10.1016/j.jom.2010.12.008.

[23] C. Kanzian, M. Kühmaier, J. Zazgornik, and K. Stampfer, "Design of forest energy supply networks using multi-objective optimization," *Biomass and Bioenergy*, vol. 58, pp. 294–302, Nov. 2013. https://doi.org/10.1016/j.biombioe.2013.10.009.

[24] M. Roni, S. D. Eksioglu, E. Searcy, and K. Jha, "A supply chain network design model for biomass co-firing in coal-fired power plants," *Transportation Research Part E: Logistics and Transportation Review*, vol. 61, pp. 115–134, Jan. 2014. https://doi.org/10.1016/j.tre.2013.10.007.

[25] J. Kim, M. J. Realff, and J. H. Lee, "Optimal design and global sensitivity analysis of biomass supply chain networks for biofuels under uncertainty," *Computers & Chemical Engineering*, vol. 35, pp. 1738–1751, Sept. 2011. https://doi.org/10.1016/j.compchemeng.2011.02.008.

[26] L. J. Fernandes, S. Relvas, and A. P. Barbosa-Póvoa, "Strategic network design of downstream petroleum supply chains: Single versus multi-entity participation," *Chemical Engineering Research and Design*, vol. 91, pp. 1557–1587, Aug. 2013. https://doi.org/10.1016/j.cherd.2013.05.028.

[27] M. Shakhsi-Niaei, S. Iranmanesh, and S. Torabi, "Optimal planning of oil and gas development projects considering long-term production and transmission," *Computers & Chemical Engineering*, vol. 65, pp. 67–80, June 2014. https://doi.org/10.1016/j.compchemeng.2014.03.002.

[28] S. R. Shariff, N. H. Moin, and M. Omar, "Location allocation modeling for healthcare facility planning in malaysia," *Computers & Industrial Engineering*, vol. 62, pp. 1000–1010, May 2012. https://doi.org/10.1016/j.cie.2011.12.026.

[29] A. Nagurney and L. S. Nagurney, "Medical nuclear supply chain design: A tractable network model and computational approach," *International Journal of Production Economics*, vol. 140, pp. 865–874, Dec. 2012. https://doi.org/10.1016/j.ijpe.2012.07.008.

[30] C. Araz, H. Selim, and I. Ozkarahan, "A fuzzy multi-objective covering-based vehicle location model for emergency services," *Computers & Operations Research*, vol. 34, pp. 705–726, Mar. 2007. https://doi.org/10.1016/j.cor.2005.03.021.

[31] S. S. Syam and M. J. Côté, "A location–allocation model for service providers with application to not-for-profit health care organizations," *Omega*, vol. 38, pp. 157–166, June 2010. https://doi.org/10.1016/j.omega.2009.08.001.

[32] P. Mitropoulos, I. Mitropoulos, I. Giannikos, and A. Sissouras, "A biobjective model for the locational planning of hospitals and health centers," *Health Care Management Science*, vol. 9, pp. 171–179, May 2006. https://doi.org/10.1007/s10729-006-7664-9.

[33] H. K. Rajagopalan, C. Saydam, and J. Xiao, "A multiperiod set covering location model for dynamic redeployment of ambulances," *Computers & Operations Research*, vol. 35, pp. 814–826, Mar. 2008. https://doi.org/10.1016/j.cor.2006.04.003.

[34] J. E. Santibañez-Aguilar, J. M. Ponce-Ortega, J. B. González-Campos, M. Serna-González, and M. M. El-Halwagi, "Optimal planning for the sustainable utilization of municipal solid waste," *Waste Management*, vol. 33, pp. 2607–2622, Dec. 2013. https://doi.org/10.1016/j.wasman.2013.08.010.

[35] A. Nagurney and F. Toyasaki, "Reverse supply chain management and electronic waste recycling: a multitiered network equilibrium framework for e-cycling," *Transportation Research Part E: Logistics and Transportation Review*, vol. 41, pp. 1–28, Jan. 2005. https://doi.org/10.1016/j.tre.2003.12.001.

[36] Y. Zhang, G. H. Huang, and L. He, "A multi-echelon supply chain model for municipal solid waste management system," *Waste Management*, vol. 34, pp. 553–561, Feb. 2014. https://doi.org/10.1016/j.wasman.2013.10.002.

[37] B. Mathur, S. Gupta, M. L. Meena, and G. Dangayach, "Healthcare supply chain management: literature review and some issues," *Journal of Advances in Management Research*, vol. 15, pp. 265–287, Apr. 2018. https://doi.org/10.1108/jamr-09-2017-0090.

[38] A. R. B. Albarune, N. Farhat, and F. Afzal, "Valued supply chain for integrated hospital management: A conceptual framework," *International Journal of Supply Chain Management*, vol. 4, no. 3, pp. 39–49, 2015.

[39] A. Polater and O. Demirdogen, "An investigation of healthcare supply chain management and patient responsiveness," *International Journal of Pharmaceutical and Healthcare Marketing*, vol. 12, pp. 325–347, July 2018. https://doi.org/10.1108/ijphm-07-2017-0040.

[40] J. C. Papageorgiou, “Some operations research applications to problems of health care systems (a survey),” *International journal of bio-medical computing*, vol. 9, no. 2, pp. 101–114, 1978.

[41] A. Rais and A. Viana, “Operations research in healthcare: a survey,” *International transactions in operational research*, vol. 18, no. 1, pp. 1–31, 2011.

[42] B. Zahiri, R. Tavakkoli-Moghaddam, M. Mohammadi, and P. Jula, “Multi-objective design of an organ transplant network under uncertainty,” *Transportation Research Part E: Logistics and Transportation Review*, vol. 72, pp. 101–124, Dec. 2014. https://doi.org/10.1016/j.tre.2014.09.007.

[43] S. Nahmias, “Perishable inventory theory: A review,” *Operations Research*, vol. 30, pp. 680–708, Aug. 1982. https://doi.org/10.1287/opre.30.4.680.

[44] I. Z. Karaesmen, A. Scheller–Wolf, and B. Deniz, “Managing perishable and aging inventories: Review and future research directions,” in *International Series in Operations Research & Management Science*, pp. 393–436, Springer US, Oct. 2010. https://doi.org/10.1007/978-1-4419-6485-4_15.

[45] J. B. Jennings, “Blood bank inventory control,” *Management Science*, vol. 19, no. 6, pp. 637–645, 1973.

[46] P. D. Cumming, K. E. Kendall, C. C. Pegels, J. P. Seagle, and J. F. Shubsda, “A collections planning model for regional blood suppliers: description and validation,” *Management Science*, vol. 22, no. 9, pp. 962–971, 1976.

[47] B. L. Deuermeyer and W. P. Pierskalla, “A by-product production system with an alternative,” *Management Science*, vol. 24, no. 13, pp. 1373–1383, 1978.

[48] G. P. Prastacos and E. Brodheim, “PBDS: A decision support system for regional blood management,” vol. 26, pp. 451–463, May 1980. https://doi.org/10.1287/mnsc.26.5.451.

[49] M. Pratt and A. Grindon, “Computer simulation analysis of blood donor queueing problems,” vol. 22, pp. 234–237, May 1982. https://doi.org/10.1046/j.1537-2995.1982.22382224948.x.

[50] A. Katz, C. Carter, P. Saxton, J. Blutt, and R. Kakaiya, “Simulation analysis of platelet production and inventory management,” vol. 44, pp. 31–36, Jan. 1983. https://doi.org/10.1111/j.1423-0410.1983.tb04100.x.

[51] R. James and D. Matthews, “Analysis of blood donor return behaviour using survival regression methods,” *Transfusion medicine*, vol. 6, no. 1, pp. 21–30, 1996.

[52] S. H. Stanger, N. Yates, R. Wilding, and S. Cotton, “Blood inventory management: Hospital best practice,” *Transfusion Medicine Reviews*, vol. 26, pp. 153–163, Apr. 2012. https://doi.org/10.1016/j.tmrv.2011.09.001.

[53] H. Lowalekar and N. Ravichandran, “Blood bank inventory management in india,” *OPSEARCH*, vol. 51, pp. 376–399, June 2013. https://doi.org/10.1007/s12597-013-0148-z.

[54] A. Pirabán, W. Guerrero, and N. Labadie, “Survey on blood supply chain management: Models and methods,” *Computers & Operations Research*, vol. 112, p. 104756, Dec. 2019. https://doi.org/10.1016/j.cor.2019.07.014.

[55] W. P. Pierskalla, “Supply chain management of blood banks,” in *Operations Research and Health Care*, pp. 103–145, Kluwer Academic Publishers. https://doi.org/10.1007/1-4020-8066-2$_$5.

[56] R. Haijema, J. van der Wal, and N. M. van Dijk, "Blood platelet production: Optimization by dynamic programming and simulation," *Computers & Operations Research*, vol. 34, pp. 760–779, Mar. 2007. https://doi.org/10.1016/j.cor.2005.03.023.

[57] Q. Duan and T. W. Liao, "A new age-based replenishment policy for supply chain inventory optimization of highly perishable products," *International Journal of Production Economics*, vol. 145, pp. 658–671, Oct. 2013. https://doi.org/10.1016/j.ijpe.2013.05.020.

[58] D. Zhou, L. C. Leung, and W. P. Pierskalla, "Inventory management of platelets in hospitals: Optimal inventory policy for perishable products with regular and optional expedited replenishments," *Manufacturing & Service Operations Management*, vol. 13, pp. 420–438, Oct. 2011. https://doi.org/10.1287/msom.1110.0334.

[59] V. Hemmelmayr, K. F. Doerner, R. F. Hartl, and M. W. Savelsbergh, "Delivery strategies for blood products supplies," *OR Spectrum*, vol. 31, no. 4, pp. 707–725, 2009. https://doi.org/10.1007/s00291-008-0134-7.

[60] T. H. Cormen, C. E. Leiserson, R. L. Rivest, and C. Stein, *Introduction to Algorithms, Third Edition*. The MIT Press, 3rd ed., 2009.

[61] R. Ramezanian and Z. Behboodi, "Blood supply chain network design under uncertainties in supply and demand considering social aspects," *Transportation Research Part E: Logistics and Transportation Review*, vol. 104, pp. 69–82, 2017. https://doi.org/10.1016/j.tre.2017.06.004.

[62] B. Zahiri and M. S. Pishvaee, "Blood supply chain network design considering blood group compatibility under uncertainty," *International Journal of Production Research*, vol. 55, pp. 2013–2033, Nov. 2016. https://doi.org/10.1080/00207543.2016.1262563.

[63] Y. Sha and J. Huang, "The multi-period location-allocation problem of engineering emergency blood supply systems," *Systems Engineering Procedia*, vol. 5, pp. 21–28, 2012. https://doi.org/10.1016/j.sepro.2012.04.004.

[64] Z. Azarmand and E. Neishabouri, "Location allocation problem," in *Facility Location*, pp. 93–109, Physica-Verlag HD, 2009. https://doi.org/10.1007/978-3-7908-2151-2_5.

[65] M. Arvan, R. Tavakoli-Moghadam, and M. Abdollahi, "Designing a bi-objective and multi-product supply chain network for the supply of blood," *Uncertain Supply Chain Management*, vol. 3, no. 1, pp. 57–68, 2015. https://doi.org/10.5267/j.uscm.2014.8.004.

[66] Alfonso, V. Augusto, and X. Xie, "Tactical planning of bloodmobile collection systems," in *2013 IEEE International Conference on Automation Science and Engineering (CASE)*, pp. 26–31, 2013. https://doi.org/10.1109/CoASE.2013.6653957.

[67] E. Alfonso, V. Augusto, and X. Xie, "Mathematical programming models for annual and weekly bloodmobile collection planning," *IEEE Transactions on Automation Science and Engineering*, vol. 12, pp. 96–105, Jan. 2015. https://doi.org/10.1109/tase.2014.2329571.

[68] J. R. Birge and F. Louveaux, *Introduction to stochastic programming*. Springer Science & Business Media, 2011.

[69] A. Jabbarzadeh, B. Fahimnia, and S. Seuring, "Dynamic supply chain network design for the supply of blood in disasters: A robust model with real world application," *Transportation Research Part E: Logistics and Transportation Review*, vol. 70, pp. 225–244, Oct. 2014. https://doi.org/10.1016/j.tre.2014.06.003.

[70] B. Fahimnia, A. Jabbarzadeh, A. Ghavamifar, and M. Bell, "Supply chain design for efficient and effective blood supply in disasters," *International Journal of Production Economics*, vol. 183, pp. 700–709, 2017. https://doi.org/10.1016/j.ijpe.2015.11.007.

[71] B. Hamdan and A. Diabat, "A two-stage multi-echelon stochastic blood supply chain problem," *Computers and Operations Research*, vol. 101, pp. 130–143, 2019. https://doi.org/10.1016/j.cor.2018.09.001.

[72] M. Dillon, F. Oliveira, and B. Abbasi, "A two-stage stochastic programming model for inventory management in the blood supply chain," *International Journal of Production Economics*, vol. 187, no. February, pp. 27–41, 2017. https://doi.org/10.1016/j.ijpe.2017.02.006.

[73] H. Lowalekar and N. Ravichandran, "Model for blood collections management," vol. 50, pp. 2778–2784, Dec. 2010. https://doi.org/10.1111/j.1537-2995.2010.02944.x.

[74] E. Alfonso, X. Xie, V. Augusto, and O. Garraud, "Modelling and simulation of blood collection systems: improvement of human resources allocation for better cost-effectiveness and reduction of candidate donor abandonment," vol. 104, pp. 225–233, Dec. https://doi.org/10.1111/vox.12001, year = 2012.

[75] A. Nagurney, A. H. Masoumi, and M. Yu, "Supply chain network operations management of a blood banking system with cost and risk minimization," *Computational Management Science*, vol. 9, no. 2, pp. 205–231, 2012. https://doi.org/10.1007/s10287-011-0133-z.

[76] H. Heidari-Fathian and S. H. R. Pasandideh, "Modeling and Solving a Blood Supply Chain Network: An Approach for Collection of Blood," *International Journal of Supply and Operations Management*, vol. 4, no. 2, pp. 158–166, 2017.

[77] M. Fazli-Khalaf, S. Khalilpourazari, and M. Mohammadi, "Mixed robust possibilistic flexible chance constraint optimization model for emergency blood supply chain network design," *Annals of Operations Research*, vol. 283, pp. 1079–1109, Dec. 2017. https://doi.org/10.1007/s10479-017-2729-3.

[78] M. Habibi-Kouchaksaraei, M. M. Paydar, and E. Asadi-Gangraj, "Designing a bi-objective multi-echelon robust blood supply chain in a disaster," *Applied Mathematical Modelling*, vol. 55, pp. 583–599, Mar. 2018. https://doi.org/10.1016/j.apm.2017.11.004.

[79] C. Rupprecht and T. Nagarajan, *Current Laboratory Techniques in Rabies Diagnosis, Research and Prevention, Volume 2*. Elsevier, 2015. https://doi.org/10.1016/c2014-0-01041-6.