A MATHEMATICAL MODELING APPROACH FOR MANAGING REGIONAL BLOOD BANK OPERATIONS

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We certify that we have read this thesis and that in our opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Master of Science.

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ABSTRACT

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Blood bank operations are complex affairs since they involve supply chain management of highly perishable goods such as whole blood and blood products. The Turkish Red Crescent (TRC), who is the main responsible organization in Turkey for collection, testing, separation and distribution of whole blood and blood products, is in constant need of optimizing its operational decisions.

We propose a mathematical modeling approach for managing the blood bank operations in the TRC that include the decisions of donation collection, production and distribution to demand points (hospitals). The model minimizes system cost while ensuring maximum level of demand satisfaction. For this purpose, a lexicographic approach is used that first determines the maximum amount of demand that can be satisfied and then solves a cost minimization model, which is a linear mixed-integer programming model. Observing that it may not be possible to find the optimal solution of this model in reasonable time for some real-life problem sizes, we develop a customized heuristic approach for the problem. We demonstrate that the heuristic algorithm provides good quality solutions in negligible time through computational experiments.

We finally examine a bi-objective extension of the cost minimization problem, where the quality of the separated blood product is considered alongside system cost. We solve the resulting bi-objective programming problems using the $\mathcal{E}-$ Constraint Method. This extension allows the decision maker to observe the trade-off between cost and quality and implement her most preferred solution among the non-dominated solutions.

Keywords: Blood bank operations, Blood platelets, Bi-objective optimization, Epsilon constraint method.

ÖZET

BÖLGESEL KAN BANKASI OPERASYONLARININ YÖNETİMİ İÇİN MATEMATİKSEL MODELLEME YAKLAŞIMI

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Kan bankası operasyonları, tam kan ve kan ürünleri gibi yüksek derecede bozulabilir ürünlerin tedarik zinciri yönetimini gerektirdiği için oldukça karmaşıktır. Türkiye genelinde tam kan ve kan ürünlerinin toplanması, test edilmesi, ayrıştırılması ve dağıtımı konusunda faaliyet gösteren Türk Kızılayı, operasyonel kararlarını sürekli olarak eniyileme ihtiyacı duymaktadır.

Türk Kızılayı'nın, bağış toplama, üretim ve hastanelere dağıtım kararlarını içeren kan bankası operasyonlarını yönetebilmesi için bir matematiksel modelleme yaklaşımı geliştirilmiştir. Önerilen model, mümkün olan en yüksek talep miktarını en az maliyetle karşılamaktadır. Bu amaçla, öncelikle, karşılanabilecek en yüksek talep miktarını belirleyen, sonrasında karışık tamsayılı bir maliyet enazlama problemi çözen bir sözlüksel yaklaşım kullanılmıştır. Bu modelin makul sürelerde çözülmesinin mümkün olmadığı gerçek hayat problem boyutları için bir sezgisel yaklaşım geliştirilmiştir. Sezgisel yaklaşımın çok kısa sürelerde kaliteli çözümler bulduğu, yapılan sayısal deneylerle gösterilmiştir.

Son olarak, kan ürünlerinin kalitesinin enbüyüklenmesi amaç fonksiyonu, maliyet enküçüklenmesi amaç fonksiyonuyla birlikte incelenmiştir. Elde edilen iki amaçlı programlama problemi $\mathcal{E}-$kısıtı yöntemi ile çözülmüştür. Bu iki amaçlı yaklaşım, karar vericinin kalite ve sistem maliyeti arasındaki ödünleşmeyi gözlemleyerek en çok tercih ettiği baskın çözümü uygulamasına olanak sağlamaktadır.

Anahtar sözcükler: Kan bankası operasyonları, Trombosit süspansiyonu, İki amaçlı eniyileme, Epsilon-kısıt yöntemi.

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Chapter 1

Introduction

Most of the studies on problems of inventory and supply chain management in the literature assume that items have infinite shelf-life and can be stocked indefinitely. However, this not the case for some types of items which lose their suitability for use, partially or entirely. For instance foodstuffs, photographic films and medicines are perishable (unfit to consume) after a given time and must be discharged from inventory without fulfilling any demand. This perishability issue often complicates the inventory and supply chain management problems. Other perishable items which are popular in the literature are whole blood and blood products (major components of whole blood).

Each year, millions of people need blood transfusions for treatment. The only sources of blood are voluntary donors since no other organic or synthesized material can as yet be used as a substitute for blood. Ensuring adequate supply is also of vital importance since patients may lose their lives in case of inadequacy of supply. The fact that donations are the only sources and very high service levels are needed, makes blood a unique product from both supply and demand aspects.

Blood donations are generally made as whole blood, which is the unseparated form of the donated resource. After collection, the whole blood is separated into its major components: red blood cells, blood plasma and blood platelets (also known as *Thrombocyte Suspension*). Hereinafter, we refer to these components as blood products. Each blood product is perishable to varying degrees and are used in the treatment of different diseases. For instance, red blood cells and blood platelets are used in treatment of patients that have sustained major blood loss. On the other hand, blood platelets are also needed for cancer treatments [2] and blood plasma is used to control severe blood loss during surgeries. The shelf lives and storage conditions also vary across different products. For example, blood platelets must be agitated gently and continuously at room temperature ($20 - 24°$C) in order to be able to stored for up to their shelf-life, which is 5 days [3]. This shelf life begins with drawing whole blood from voluntary donors. The shelf life is much longer for red blood cells and plasma. Under proper conditions, ($2 - 6°$C) red blood cells can be stored up to 42 days and plasma ($\leq -25°$C) can be stored up to 12 months in frozen form. Hence, among these major components, blood platelets are the most perishable.

Blood bank services constitute a crucial part of the national health care system of Turkey. The Turkish Red Crescent (TRC), which is the society that has been serving in this area since 1950s, is the most authoritative institution in this field throughout the country. The society takes "Providing aid for needy and defenseless people in disasters and usual periods as a proactive organization,developing cooperation in the society, providing safe blood and decreasing vulnerability"[4] as their mission they fulfill most of the demand for blood products of the country. Hence the success of the overall healthcare system depends crucially on the performance of the blood supply services that the TRC provides.

In this thesis, we investigate the problem of determining schedules of blood collections and blood tests so as to minimize cost and maximize quality while ensuring the minimum level of total unsatisfied demand (TUD). The aim of this study is to develop an easy-to-use method that creates the schedules. We propose a mathematical modeling based approach and report on the performances of various exact and heuristic solution methods used to solve these models.

In the following chapter, we first describe the blood bank system of TRC to go along with statistical data pertaining to blood services of the TRC and explain the elements of the system, their responsibilities and the relationship between them. Then we introduce the problem that we focus on in the scope of this thesis. Particular emphasis is given on the internal procedures of TRC and system/modeling limitations based on these internal procedures for the purposes of constructing a system as close to the reality of TRC operations as possible.

In chapter 3, we review the most relevant studies in literature and point out the main contributions of our work. The majority of literature is was devoted to ordering/production size determination, issuing and scheduling problems, although attention has also been given to transshipment, location-allocation and vehicle routing problems. A few studies focus in particular on TRC blood services.

In chapter 4, we discuss the main mathematical model and the lexicographic approach we propose. We first minimize TUD, after which we solve a second model that minimizes cost while ensuring that the TUD is kept at its minimum. We refer to this model as the *cost minimization model*. We then discuss the solution approaches used. This chapter also includes the computational studies performed to test the performance of the approaches.

In chapter 5, a bi-objective extension of the cost minimization model is proposed that maximizes separation-age-based quality of blood products alongside minimization of cost subject to the same constraint that TUD is kept at its minimum level. The solution method, the $\mathcal{E}$-Constraint Method, that we have used for this bi-objective programming problem is presented and briefly explained in this chapter. A sample Pareto-chart and results of the computational experiments are also provided.

In chapter 6, we conclude the discussion by proving a brief overview of the study done and discussing some future work directions.

Chapter 2

System Description and Problem Definition

Blood bank services are being run by Red Crescent and Red Cross organizations in many countries [5]. Likewise, in Turkey, this service is run and managed by the Turkish Red Crescent (TRC). To manage this complicated system, TRC operates in 17 Regional Blood Centers (see Figure 2.1 for blood donation percentages for each region), each with its own responsibility area and equipments. Although it is not the largest center, the Middle Anatolian Blood Center in Ankara is the main headquarters. The list of the RBCs and their aggregated amount of blood donations in 2016 are shown in Table 2.1.

The blood collection and distribution system of TRC consists of four main elements: Blood Collection Centers (BCC), Regional Blood Centers (RBC), Laboratories (Lab) and Hospitals (H). TRC collects the blood donations at the BCCs. Then, the donated blood is sent to the RBC to which the BCC is assigned. Each RBC acts as a storehouse for the BCCs in its area of responsibility. The stored blood is then sent to a lab to which the RBC is assigned. The role of the labs in the system is performing the necessary blood tests and separating the blood into its products, such as red blood cells, blood plasma and blood platelets/thrombocyte suspension (TS). The last step is satisfying the demands of the hospitals assigned to the lab by sending the demanded blood products.

Table 2.1: Locations of Regional Blood Centers and Amount of Blood Donations in 2016

RBC	Location	Total Number of Blood Donations in 2016
Aegean	İzmir	345,435
Europe	İstanbul - Bağcılar	238,531
Middle Anatolian	**Ankara**	**216,642**
Middle Mediterranean	Adana	191,242
Eastern Mediterranean	Gaziantep	153,851
Southern Marmara	Bursa	135,507
Northern Marmara	İstanbul - Kartal	123,563
Western Blacksea	Düzce	114,452
Central Anatolian	Kayseri	107,922
Mediterranean	Antalya	103,665
Middle Blacksea	Samsun	92,923
Western Anatolian	Eskişehir	79,180
Eastern Blacksea	Trabzon	58,101
Southwest	Malatya	57,787
Eastern Anatolian	Erzurum	51,874
Southern Anatolian	Diyarbakır	39,066
Southeast	Van	32,024

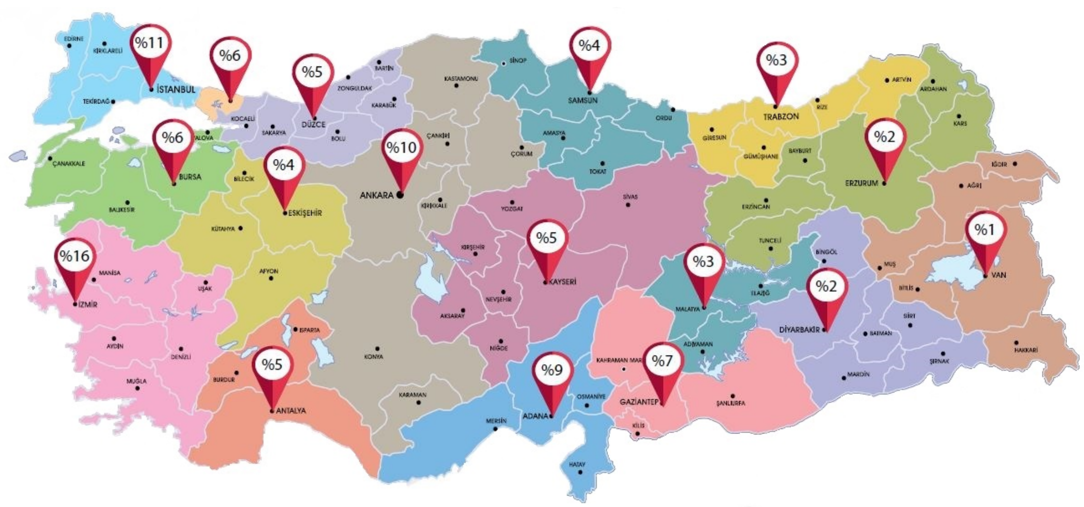

Figure 2.1: Map of the 17 Blood Regions With Blood Donation Percentages in 2016 [1]

In the current system, each BCC is assigned to a single RBC and each RBC is assigned to a single lab. There are two kinds of Regional Blood Centers, the ones with their own lab and the ones without. The RBCs without a lab are assigned to other RBCs' labs. In this work, we considered an RBC with its own lab and made our analysis accordingly. We constructed our mathematical model to optimize the processes of an RBC with its own lab, and its assigned BCCs, RBCs, Lab and Hospitals. Figure 2.2 depicts the system elements as well as the main product and information flows.

As mentioned, the model that we constructed is based on a single RBC with its own lab. For the sake of simplicity, we define an aggregated system and take all RBCs and BCCs that are assigned to the RBC of concern as a single (aggregated) collection center. Similarly, the hospitals assigned to the RBC are considered as a single hospital (an aggregated demand node). (See Figure 2.3) Hence, the aggregated version consists of one Blood Collection Center, one Regional Blood Center with a lab and one hospital, as shown in Figure 2.4.

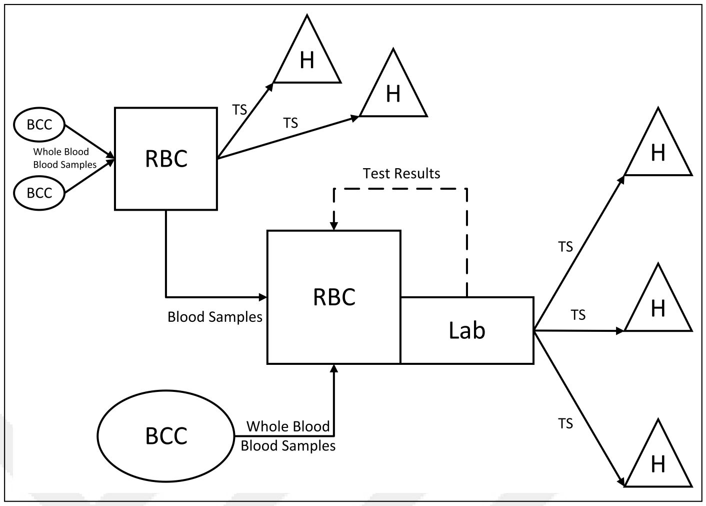

Figure 2.2: System Design

This aggregation method assumes that collection from any BCC takes the same amount of time. Also it assumes that the time it takes to transfer blood in the following two ways is the same: BCC-RBC (without lab)-RBC (with lab) and BCC-RBC (with lab). It is possible to relax these assumptions and use a specific collection duration and a specific collection schedule for each of the BCCs and RBCs that are assigned an RBC that has a lab. This method, however, would require detailed information on collection processes and durations, which is not the case for this study. As a result, we use the aggregation method shown in Figure 2.3.

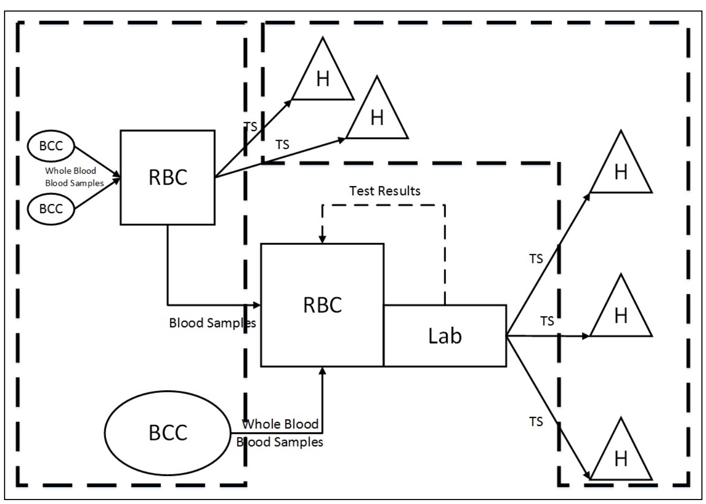

Figure 2.3: Aggregation of the System Design

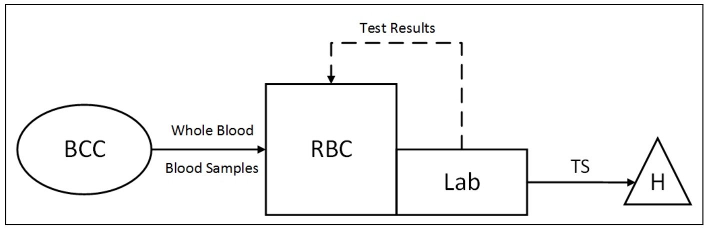

Figure 2.4: Aggregated System Design

With 2,141,765 bags of whole blood donations and 3,674,477 satisfied blood product demands in 2016, the TRC has taken one step closer to reaching the goal of collecting all of the nation's blood donations and meeting all of the demand for blood and blood products in Turkey [1] (To see the changes in the total amount of blood donations over the years, please see Figure 2.5). To achieve this goal, TRC collects blood donations through 17 RBCs, 64 BCCs and over 150 mobile blood donation units [4]. In addition to this, with their 5 laboratories that work 24 hours and all 7 days of the week, TRC performs over 6000 blood tests on average every day [1].

Managing such a large and complicated system is costly, hence the TRC is required to make good operational decisions to keep the cost as minimum as possible without conceding from service capacity. One of the main cost items is due to disposal: every year a significant percentage of blood products is disposed for various reasons. In 2016 this percentage was higher than 16% for TS. (See Figure 2.6 to see the changes in the total amount of disposed TS). Considering the fact that there is not enough donation to meet demand in full, this result is quite undesirable.

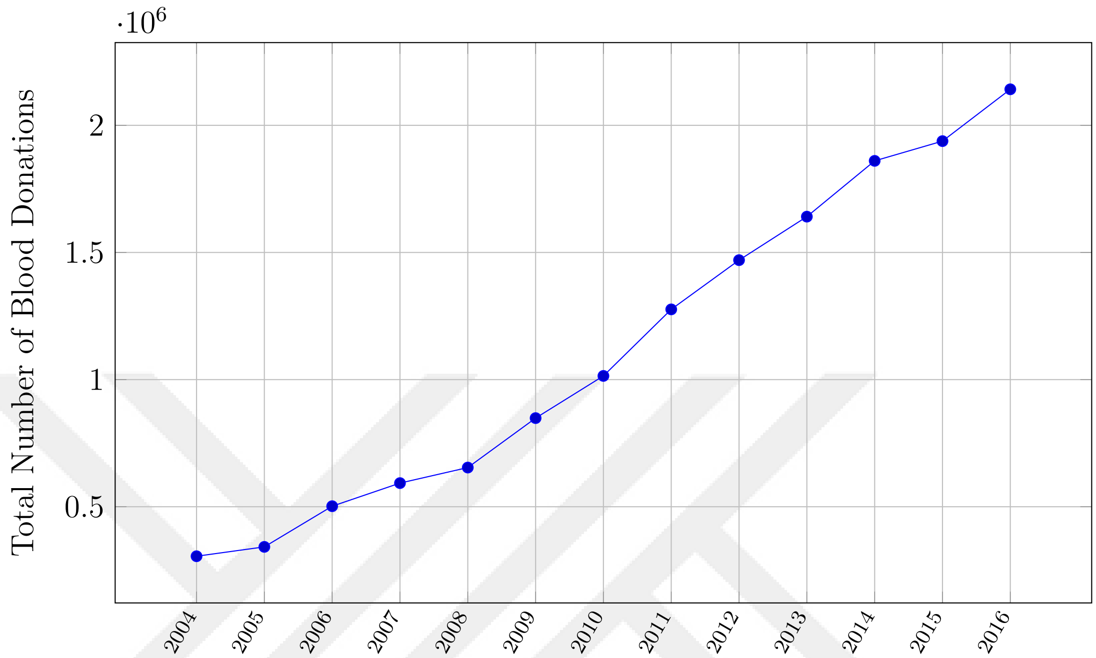

Figure 2.5: Total Number of Blood Donations 2004-2016 [1]

There is need for a decision support system that helps the decision makers in the TRC to make collection and delivery decisions of blood samples to laboratories and blood products to hospitals so as to minimize the system cost and maximize the demand fulfillment. For this purpose, we suggest an optimization based system that solves mathematical models to minimize the total cost of the system. The proposed approach may be used for any type of blood product. However, we demonstrate its use for the TS-related decisions since TS is the product with shortest shelf life, which is only 5 days under proper storage conditions, which we are assuming are being upheld by TRC for the purposes of this study. From now on, the expression "blood products" will be used to address TS. We assume that the total cost of the system is the sum of disposal, inventory, delivery and test costs. These cost items will be detailed below.

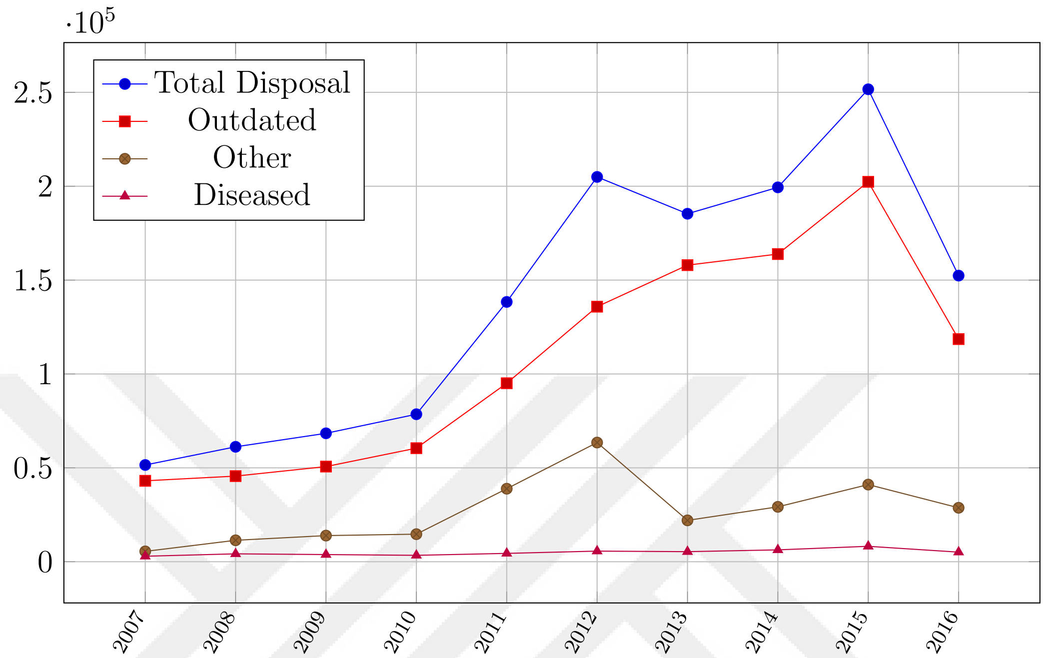

Figure 2.6: Total Number of TS-Disposals 2004-2016 [1]

To minimize outdated product rate we minimize *disposal cost*: we incur a penalty for each unit of disposed blood product; disposal cost is the total penalty incurred. The total cost function also includes the cost of delivery and test. The inventory cost stands for the holding cost of blood products, in our case TSs. The holding cost of whole blood is ignored since it is relatively low on unit base compared to the other cost items, according to the information we received in our meetings with the decision makers in TRC. In these interviews we also received detailed information on the operational facts and rules that we need to consider while creating the models. These are as follows:

Although the shelf-life of TS is declared as 5 days, hospitals do not accept any blood products on the last day of its shelf life (the day before its expiration date). In other words, at the end of day 4, TSs become useless. In line with this observation, we also assume that after 4 days, blood products perish and will be disposed, which incurs cost.

According to the demand satisfaction policy of TRC, any demand must be satisfied within 24 hours, otherwise TRC has to authorize the hospital to collect blood donations as much as is needed and to perform the necessary blood tests. Hence, in the model there is a 24 hours time limit for backorder. In the following chapters we will also discuss the impact of this policy on model performance.

The TRC stores the collected whole blood donations in a depot for a maximum duration of 24 hours. The 24-hour time limit is justified as thus: 24 hours after the donation is drawn, whole blood runs the risk of bacterial contamination [6], in which case the donation is no longer usable and is deemed perished. Therefore, the TRC either separates the whole blood, or failing to do so, disposes of the whole blood after 24 hours. Therefore, especially considering that TRC storage capacity is far above any daily donation amount, it is safe to assume that such a quick circulation of whole blood donations ensures that there is always sufficient storage space.

This thesis has been prepared in accordance with information received from the TRC with respect to its internal procedures, for the purposes of optimizing the transit of whole blood and its samples from BCC to RBC and Labs, as well as the scheduling of the testing and separation of the blood donation. The study therefore focuses on TRC procedures. For the purposes of further applying the methods herein to other blood bank organizations, our working assumptions may not hold true. Nevertheless, we propose a method that will be applicable with some variation to blood bank and other perishables applications.

Chapter 3

Literature Review

In this section, we discuss the relevant part of the literature on the application of Operations Research and Management Science methods to inventory and supply chain management problems of perishable items. The review paper by Nahmias [7] shows that these problems have motivated researchers since the mid-1950s. In these studies, inventory and supply chain management systems of foodstuffs, medicines, photographic films and blood products were analyzed [7]. In particular, a 1960s research on supply chain management of blood and blood products has made valuable contributions to the development of effective policies for perishable inventory systems [7].

An important part of the literature on blood supply chain has been developed in the 1970s and 1980s [8]. Nevertheless, this research area is still popular today and every year, dozens of studies are added to the literature. The interested reader is referred to the review papers of Beliën and Forcé [2], Osorio et al. [8] and Janssen et al. [9], for more information on the relevant problems and solution approaches on blood supply chain design.

In the following, some notable studies that are conducted on inventory and supply chain management problems are briefly discussed. These studies focus on different decisions made in supply chain and logistics systems, hence the types of the problems that have been made subject to the literature constitute a wide range from ordering/production size determination ([10], [11], [12], [13], [14], [15], [16]), scheduling ([17], [18], [19]), issuing ([13], [15], [20], [21], [22], [23], [24]), transshipment ([25]), location-allocation ([19], [26]) and vehicle routing ([13], [27]). In addition, studies that are conducted on the TRC blood services ([26], [28]) will be reviewed. Table 3.1 summarizes these studies.

A well-known problem that is addressed in the relevant literature is determining order/production size. One of the fundamental studies in this field was prepared by Hsu [10], in which an economic lot size (ELS) model for perishable goods is discussed. The author focuses on cases where the conventional ELS approaches cannot be implemented. For such cases, a new model with general concave manufacturing and stock cost functions is presented. It is assumed that the inventory in hand generates a holding cost that is in proportion to the age of the inventory. By analyzing and making good use of the optimal outcomes of the model, a dynamic programming algorithm is developed in order to solve the problem in polynomial time. The performance of the algorithm is put to trial on various cases. A computational complexity reduction technique was applied in some cases to obtain a solution in reasonable time.

Minimization of shortage and wastage are two of the most discussed objectives for blood supply chain management problems in the literature. As a consequence of perishability of blood and blood products, holding a large number of items in inventory may increase wastage. On the other hand, keeping the inventory level low may cause shortages, which may have serious consequences such as increased fatality rate. Haijema et al. [11] studied the problem of minimizing shortages and wastages of blood platelets that have a limited shelf life of 5 to 7 days. The authors used a solution method that is a Markov dynamic programming coupled with a simulation approach. Due to the complexity of the problem, a downsizing method is used to find near-optimal solutions. In this study, two kinds of demands are considered; demand for young platelets and demand for platelets at any age. This is because some oncology and hematology operations can only be performed with 'young' platelets. The solution approach is illustrated on an actual case study of the Dutch Blood Bank.

Haijema et al. [12] conducted a study that aims to find the optimal production level of blood platelets and used shortage and wastage rates as system performance measures of the blood service system. The problem is investigated under an approach which couples a simulation with a stochastic dynamic programming (SDP) model. This article is mainly focused on the impacts of irregular breaks to the system performance. The term "irregular break" refers to periods where the production stops, such as Easter and Christmas holidays. The presented approach is evaluated on a stochastic environment by using real data from Northeast Dutch Blood Bank.

Another study under the topic of determining order/production size is conducted by Gunpinar [13], who studied blood supply chain management problem by focusing on minimization of shortage and wastage amounts of blood products. The author developed three mathematical models with the aim of improving the efficiency of the blood services. The first model aims to determine the optimal order quantities so as to minimize the total cost, shortage and wastage of blood. The second model is used to develop a formula for various shortage and distribution policies and the third model formulates a vehicle routing problem to minimize the traveled distance by mobile collection vehicles (bloodmobiles). Computational studies are performed to compare different solution methods with respect to solution times.

Duan and Liao [14] also addressed the problem of determining ordering policies by proposing a simulation model, which aims to minimize the expected amount of wastages while allowing a limited amount of shortages. A new age-based ordering policy is designed to determine the order/production size depending on the ratio of "old" items to the whole inventory. Here, this ratio is used as an indicator of the inventory freshness. The authors compared this approach with two order-up-to policies from the literature and concluded that the proposed policy outperforms the others.

Haijema [15] investigated the impacts of different ordering, issuing and disposal policies on inventory cost. Stochastic Dynamic Programming is used to minimize age dependent inventory cost. The authors concluded that when FIFO issuing and optimal ordering policies are being used together, the impact of optimal disposal policy is profound on reducing the cost. However, when LIFO issuing policy is used this impact is significant only when sub-optimal ordering (e.g. Base Stock Policy) policies are used.

Gunpinar and Centeno [16] conducted a study to handle the two contradicting matters, shortages and wastages. They proposed integer programming (IP) models aimed to minimize the total cost of the system, which includes penalty costs of wastage and shortage, by determining the optimal ordering levels. In this study, the authors focused on blood products such as red blood cells and blood platelets. The models were evaluated under stochastic and deterministic demand assumptions and the computational results were presented.

Another extensively-studied problem type in the related literature is the scheduling problem. In 2010, Ghandforoush and Sen [17] created a decision support system in order to optimize the production process of thrombocyte and the schedule of blood collecting vehicles. The system uses a non-convex integer optimization model, which is linearized by a two-step conversion technique to reduce complexity. The authors also provided the computational results of the designed system for test data.

Alfonso et al. [18] addressed the scheduling problem of collection vehicles in two parts. They first conducted a study that determines the weeks of collection for each region in the system such that each one of them will become self-sufficient for the whole year. At the second part of this study, the weekly scheduling problem of bloodmobiles was investigated to determine their work days. In total three Mixed Integer Programming (MIP) models have been presented: Two models are presented for the first part of the study and another one for the second part. These models were evaluated using real-life data from Auvergne-Loire Region of French Blood Services. Beside these models, a new approach was designed to estimate the amount of blood donations by taking the following factors into account: population demographics, generousness and accessibility of donors.

In most of the papers, whole blood and/or major blood components (red blood cells, blood plasma and blood platelets/thrombocytes) are the main focuses at the development stage. On occasion, sub-products have been chosen as well. Sub-products are also blood products that are produced by processing the major components. As an example, the study of Ayer et al. [19] is based on "cryoprecipitate". Cryoprecipitate is a sub-product of blood plasma which plays a crucial role when dealing with massive bleeding cases. During this study, the authors worked in cooperation with the American Red Cross (ARC) to determine the right times and the right mobile collection sites to collect blood so that the weekly collection goal is reached, cryoprecipitate production is made and the collection costs are kept at minimum. To formulate the system, a mathematical model is developed. Unlike many other blood products that can be produced within the 24-hours of collection [6], cryoprecipitate units can only be produced within 8 hours. This restriction increases the complexity of the problem exponentially and renders the problem difficult to solve by classical dynamic programming solution approaches. Thus, a heuristic algorithm was developed and used in conjunction with the model to find near-optimal solutions. The authors demonstrate applicability of the proposed approach via computational studies and a pilot scheme on the real system of ARC.

Pierskalla and Roach [20] analyzed the performances of the issuing policies FIFO (demand is satisfied by the oldest item on hand) and LIFO (demand is satisfied by the youngest item on hand) under various objectives such as maximizing the total utility of the system, minimizing the total lost/backlogged demand and minimizing the total wastage. It is assumed that demand received for an item at a particular age can only be satisfied with items at that age or younger ones. Under this assumption, issuing policies are compared for both backlogged and lost demand cases. The results show that for most of the cases FIFO is the best option for inventory systems of perishable items.

Another study that investigated the effects of issuing policies on perishable inventory systems is done by Parlar et al. [21]. In this study, authors compared the two pure issuing policies for perishable items: FIFO and LIFO. They compare the policies with respect to expected average profit in the long run, which is a function of purchase cost, shortage penalty, holding cost and earned revenue. The authors provided analytical results and performed a sensitivity analysis for different parameters.

Abdulwahab and Wahab [22] studied the inventory problem of blood platelet bank with consideration of eight blood types and stochastic demand and supply. The authors formulated the problem using approximate dynamic programming and used shortage, outdating, stock level and reward gained as the performance criteria. They investigate substitution relationships of blood types and derive a reward function that promotes satisfaction of demands with the same blood type and also allows demand satisfaction with different blood types. The authors stated that the shortage penalty should be at least 5 times that of disposal penalty in order to ensure that no demand is lost when there is sufficient inventory. (However, our computational studies shown that this ratio does not guarantee the preferred result. According to our experiences this ratio should be much higher) They conducted computational studies to investigate the effect of optimal inventory level on the performance criteria.

Abbasi and Hosseinifard [24] addressed the problem of determining the optimal issuing policy for perishable inventory systems under supply uncertainty. Since especially young blood products are needed for some treatments, the authors aim to reduce the age of goods to be provided to hospitals along with waste and shortage minimization. The authors propose a new issuing policy, which divides the inventory in two parts using a threshold age. Let S_1 be the "younger" division and S_2 be the "older". Whenever a demand is received, it is satisfied with goods from set S_1, as long as it is not empty. Otherwise the set S_2 will be used. The pure FIFO policy will be used within each set. The computational studies show that the modified policy surpasses pure LIFO and FIFO policies in terms of performance measures.

There are also studies in the literature that focus on distinct aspects of blood related logistics systems. Wang and Ma [25] investigate the interaction between blood banks in a blood bank logistics system and optimize the inventory exchange between them. The authors analyzed the transshipment problem of blood banks in the event of scarcity. Scarcity can be of three types: regional, structural and seasonal. This study is conducted on a system that includes two types of blood banks: “affected” and “rescue”. A blood bank is referred to as ”affected” when there is shortage within its region and blood transshipments will be made from rescue blood banks located in other regions. The authors presented an age-based policy instead of a quantity-based one and declared that it is capable of minimizing wastage rate more successfully under FIFO issuance policy. Simulation studies of the proposed age-based transshipment model are presented and sensitivity analysis is performed.

Şahin et al. [26] conducted a study on the location-allocation problem of the Turkish Red Crescent. The aim of the study is to determine locations of regional blood centers and allocation of blood collection centers and hospitals to the regional blood centers. 3 mathematical models are proposed for this purpose. The performances of these models are evaluated using real data.

Randa et al. [28] performed a study at the Turkish Red Crescent to minimize the shipping durations of blood products from regional blood centers to demand nodes, e.g. hospitals. In order to improve the system performance, the authors recommended a new facility type to be built between the regional blood centers and the demand nodes, which they call “distribution centers”. The authors therefore proposed to add a fourth level to the current 3-level-system. The performance of the proposed system is evaluated with a simulation model that considers all three major blood products and the results are compared with the real life data of the Turkish Red Crescent.

Table 3.1: Relevant Studies in the Literature

Study	Problem Type	Solution Method	Main Decision(s)	Objective(s)	Blood Product
Hsu [10]	Order Size	Dynamic Programming Algorithm	Determining Order Quantity	Min Cost	×
Haijema et al. [11]	Production Size	Markov Dynamic Programming & Simulation	Determining Production Level	Min Shortage Min Wastage	Blood Platelets
Haijema et al. [12]	Production Size	Stochastic Dynamic Programming & Simulation	Determining Production Level	Min Shortage Min Wastage	Blood Platelets
Gunpinar [13]	Order Size	Integer Programming	Determining Order Quantity	Min Cost Min Shortage Min Wastage	Blood Platelets & Red Blood Cells
	Issuing	Integer Programming	Determining Issuing and Shortage Policies	Min Shortage	Blood Platelets & Red Blood Cells
	Vehicle Routing	Integer Programming	Determining The Route of Bloodmobiles	Min Total Traveled Distance	Blood Platelets & Red Blood Cells
Duan and Liao [14]	Order Size	Metaheuristic Simulation Approach	Determining Replenishment Policy	Min Total Expected Wastage	×
Haijema [15]	Order Size & Issuing	Dynamic Programming	Determining Ordering, Issuing, Disposal Policies	Min Age Dependent Inventory Cost	×
Gunpinar and Centeno [16]	Order Size	Integer Programming	Determining Order Quantity	Min Cost Min Shortage Min Wastage	Blood Platelets & Red Blood Cells
Ghandforoush and Sen [17]	Collection & Production Scheduling	Linearized Integer Programming	Determining Collection Schedule of Bloodmobiles	Min Cost	Blood Platelets
Alfonso et al. [18]	Collection Scheduling	Mixed Integer Programming	Determining Collection Schedule of Bloodmobiles	Min Cost	Whole Blood
Ayer et al. [19]	Collection Scheduling	Dynamic Programming Algorithm	Determining Collection Schedule of Bloodmobiles	Min Collection Cost	Cryoprecipitate
Pierskalla and Roach [20]	Issuing	Mathematical Model	Determining Issuing Policy	Max Utility Min Backlogged Demand Min Wastage	Whole Blood
Parlar et al. [21]	Issuing	Mathematical Derivations	Determining Issuing Policy	Max Expected Average Profit	×

Study	Problem Type	Solution Method	Main Decision(s)	Objective(s)	Blood Product
Abdulwahab and Wahab [22]	Issuing	Aproximate Dynamic Programming	Determining Issuing Policy	Max Net Reward	Blood Platelets
Duan and Liao [23]	Issuing	Simulation-Based Heuristic Algorithm	Determining Issuing Policy	Min Expected Rate of Outdated Demand	Red Blood Cells
Abbasi and Hosseinifard [24]	Issuing	Performance Approximation Methods & Simulation	Determining Issuing Policy	Min Average Age of Issue	Blood Platelets & Red Blood Cells
Wang and Ma [25]	Transshipment	Simulation Model	Determining Inventory Exchange Level Btw RBCs	Min Wastage	Red Blood Cells
Şahin et al. [26]	Location Allocation	Integer Programming	Determining Location of RBCs & Allocation of Facilities	Min Total Weighted Distance Min Number of Stations Max Weighted Fleet Size	×
Randa et al. [28]	System Design	Simulation Model	Determining Locations of new Distribution Centers	Min Average Shipping Duration	×

It is seen that most of the current studies in the literature address problems of inventory and logistics systems of blood banks. However, to the best of our research, there are no studies that aim to optimize both collection and production schedules of perishable items to be used on a daily basis in blood bank systems. We aim to fill this gap by proposing a modeling approach to help decision makers with collection and production decisions that minimize cost and also takes production-age-based quality of the produced items into account. To the best of our knowledge, this is the first study that handles these two objectives simultaneously in blood bank settings.

Chapter 4

Cost Minimization Setting

TRC provides healthcare services in a variety of different fields and efficient use of resources is therefore of utmost importance for it to effectively provide these services. Due to these efficiency concerns, cost minimization becomes increasingly important for the TRC in its blood product delivery system. Naturally, given the importance of the proper delivery of the product that the TRC ultimately provides, cost minimization at the expense of demand satisfaction is out of the question for the TRC. Hence we first create a model that aims to maximize demand fulfillment (that is to minimize total unsatisfied demand (TUD)) for a limited time horizon, after which we find the minimum cost arrangement with the same TUD level by solving a second mathematical model.

In this chapter, we first introduce the modeling assumptions and the notation used in the models. We then present our first model that minimizes the total unsatisfied demand (TUD) for thrombocyte suspension (TS). The second model that minimizes the total cost while ensuring that the TUD is at the minimum level possible is then proposed. These two models constitute a single lexicographic bi-objective model. We investigate various exact and heuristic approaches to find optimal and heuristic solutions to these models. We conclude the chapter by presenting the results of the computational studies used to test the performance of the approaches.

4.1 Mathematical Models

In this section, a list of assumptions that we have used and the reasons behind them are presented first, followed by the notation that is used in the models. The assumptions are validated in the meetings held with authorities in the TRC.

Assumptions:

1. It is assumed that both labs and vehicles (bloodmobiles) have infinite capacity. This assumption does not harm the practicality of our models since the capacity of the labs and collection vehicles of the TRC are significantly higher than the amount of blood donations in any region.
2. As can be seen in Figure 2.6, more than 99% of the blood samples pass the laboratory tests and this rate is getting higher every year. This is a result of the infectious disease monitoring policy of the TRC. Once a person is identified as infected, the TRC adds him/her to its infected persons list and does not accept blood donations from that person again. Therefore, it is assumed that 100% of the blood samples (donations) pass the laboratory tests.
3. Separation of whole blood into blood products takes less time than the blood tests and these two procedures can be done simultaneously. Hence we assume that by the time the tests are performed, the blood products are already ready for delivery.
4. It is assumed that once a test or collection decision is made, the whole stock which is ready to be operated will be collected or tested.
5. Total durations of test and collection activities are constant and known.
6. Operating costs of the lab for 1 hour and transportation (collection) costs of the TRC for 1 hour are fixed and known.
7. Since the system is considered to be an aggregated system, there is only 1 hospital and 1 BCC which is assigned to an RBC with its own lab.

The following notation will be used hereafter:

Sets: $P = \{1, \ldots, P_m\}$: The set of periods

Parameters:

P_m : The total number of periods in the planning horizon

A : Duration of collection, in terms of periods

BO : Time limit to satisfy a demand, in terms of periods (For $BO = 1$ a demand must be satisfied at the period that the demand occurs (No-Backoder Policy))

M : Duration of tests, in terms of periods

N : Total lifetime of TS (5 Days), in terms of periods

G : Equals 1 day, in terms of periods

P_H : The holding cost of the blood products for 1 period, per ml.

P_D : The cost of disposing the blood products, per ml.

P_O : The operation cost of the laboratory for performing blood tests and producing the blood products, per period

P_C : The collection cost of the vehicles that collect the whole blood (blood samples) from the blood collection centers (other RBCs), per period

B_p : Total amount of blood donations at period p (in terms of ml.)

T_p : Total demand for TS at period p

U : A general upper bound for the amount of product in the system

Decision Variables:

$C_H =$ Total holding cost of blood products

$C_D =$ Total disposal cost of perished blood products

$C_O =$ Total operating cost of the lab

$C_C =$ Total collecting cost of whole blood (blood samples) from the blood collection centers (other RBCs) to the regional blood center

$$W_p = \begin{cases} 1 & \text{if the donations are collected from the BCCs to the RBC in period } p \\ 0 & \text{o.w} \end{cases}$$

$$Z_p = \begin{cases} 1 & \text{if the lab performs tests and produces the blood products in period } p \\ 0 & \text{o.w} \end{cases}$$

$G_{p,t} =$ The amount of whole blood at age t that is not collected at the beginning of period p (ml.)

$X_{p,t} =$ The amount of whole blood at age t that is collected but not tested at the beginning of period p (ml.)

$Y_{p,t} =$ The amount of blood products (TS) at age t that is just tested at the beginning of period p (ml.)

$F_{p,t} =$ The amount of stock that we have at at the end of the period p and age t (inventory) (ml.)

$SV_{p,t,k} =$ The amount of TS that has been delivered to hospitals at period p and age t to satisfy the demand created in period k (ml.)

$E_p =$ The amount of unsatisfied demand at the end of the period p (ml.)

$H_{p,t} =$ Dummy variable used for linearization purposes ($W_p \times G_{p,t}$)

$D_{p,t} =$ Dummy variable used for linearization purposes ($Z_p \times X_{p,t}$)

We first solve the following model that minimizes total unsatisfied demand. The solution of this model will be an input for the other models.

$$min \quad \sum_{p=1}^{P_m} E_p \tag{4.1}$$

$s.t$

$$G_{p,1} = B_p \qquad \forall p \in \{1, \ldots, P_m\} \tag{4.2}$$

$$G_{p+1,t+1} - G_{p,t} + (W_p \times G_{p,t}) = 0 \qquad \forall p \in \{1, \ldots, P_m - 1\}, t \in \{1, \ldots, G - M - A\} \tag{4.3}$$

$$X_{p+1,t+1} - X_{p,t} - (W_{p+1-A} \times G_{p+1-A,t+1-A}) + \ldots$$
$$\ldots + (Z_p \times X_{p,t}) = 0 \qquad \forall p \in \{1 + A, \ldots, P_m - 1\}, t \in \{1 + A, \ldots, G - M\} \tag{4.4}$$

$$X_{p+A,1+A} - (W_p \times G_{p,1}) = 0 \qquad \forall p \in \{1, \ldots, P_m - M - A\} \tag{4.5}$$

$$Y_{p+M,t+M} - (Z_p \times X_{p,t}) = 0 \qquad \forall p \in \{1 + A, \ldots, P_m - M\}, t \in \{1 + A, \ldots, G - M\} \tag{4.6}$$

$$Y_{A+M+1,t} - \sum_{k=p-BO+1}^{p} (SV_{A+M+1,t,k}) - F_{A+M+1,t} = 0 \quad \forall t \in \{A + M + 1, \ldots, G\} \tag{4.7}$$

$$Y_{p,A+M+1} - \sum_{k=p-BO+1}^{p} (SV_{p,A+M+1,k}) - F_{p,A+M+1} = 0 \quad \forall p \in \{A + M + 1, \ldots, P_m\} \tag{4.8}$$

$$F_{p-1,t-1} + Y_{p,t} + \sum_{k=p-BO+1}^{p} (SV_{p,t,k}) + F_{p,t} = 0 \qquad \forall p \in \{A + M + 2, \ldots, P_m\}, t \in \{A + M + 2, \ldots, G\} \tag{4.9}$$

$$F_{p-1,t-1} + \sum_{k=p-BO+1}^{p} (SV_{p,t,k}) + F_{p,t} = 0 \qquad \forall p \in \{A+M+2,\dots,P_m\},$$

$$t \in \{G+1,\dots,N-G\} \tag{4.10}$$

$$E_p = T_p \qquad \forall p \in \{1,\dots,A+M\} \tag{4.11}$$

$$E_p + \sum_{t=A+M+1}^{N-G} \sum_{s=p}^{p+BO-1} SV_{p,t,k} = T_p \qquad \forall p \in \{A+M+1,\dots,P_m-BO+1\} \tag{4.12}$$

$$E_p + \sum_{t=A+M+1}^{N-G} \sum_{s=p}^{P_m} SV_{p,t,k} = T_p \qquad \forall p \in \{P_m-BO+2,\dots,P_m\} \tag{4.13}$$

$$X_{p,G-M+1} = 0 \qquad \forall p \in \{1,\dots,P_m\} \tag{4.14}$$

$$G_{p,G-A-M+1} = 0 \qquad \forall p \in \{1,\dots,P_m\} \tag{4.15}$$

$$Z_p = \{0,1\} \qquad \forall p \in \{1,\dots,P_m\} \tag{4.16}$$

$$W_p = \{0,1\} \qquad \forall p \in \{1,\dots,P_m\} \tag{4.17}$$

All non-negative (4.18)

The objective function (4.1) quantifies the total amount of unsatisfied demand to be minimized subject to the problem specific constraints. The only output that will be used out of this model is its optimal objective value. This model can be seen as a generator of a feasibility condition for the other models.

Constraints (4.2) ensure that the donations enter the system as uncollected whole blood (not separated or tested yet) at age 1 in each period. Constraints (4.3) control the aging process of uncollected whole blood. Constraints (4.4) and (4.5) control the aging process of collected whole blood and the transformation of uncollected whole blood into collected ones. Constraints (4.6) control the transformation of not tested whole blood into tested and separated TSs. Constraints (4.7), (4.8), (4.9) and (4.10) are inventory balance constraints. These control the aging process of tested blood products and transmission of blood products to transfusion centers, in our case hospitals, in order to satisfy their demands. Constraints (4.11), (4.12) and (4.13) calculate the amount of unsatisfied demand in each period. The constraints (4.15) and (4.14) guarantee that there will not be any disposals before the tests. All donations in the system must be tested for contagious disease tracking purposes before the planning period ends. Finally, the constraints (4.16), (4.17) and (4.18) indicate the domains and sign restrictions of the decision variables.

As mentioned in Chapter 2, this model is constructed based on an aggregated system approach, where only 1 supply and 1 demand point are assigned to an RBC that has its own lab. This assumption can be relaxed and the system can be investigated with multiple BCCs with their specific collection durations and decisions. To do so, the above model can easily be adjusted by replacing the constraints (4.2), (4.3), (4.4) and (4.5) with the following four and adjusting the index sets of the model accordingly.

$$G_{p,1,BCC} = B_{p,BCC}$$
$$G_{p+1,t+1,BCC} - G_{p,t,BCC} + (W_{p,BCC} \times G_{p,t,BCC}) = 0$$
$$X_{p+1,t+1} - X_{p,t} - \sum_{BCC} (W_{p+1-A,BCC} \times G_{p+1-A,t+1-A,BCC}) + (Z_p \times X_{p,t}) = 0$$
$$X_{p+A,1+A} - \sum_{BCC} (W_{p,BCC} \times G_{p,1,BCC}) = 0$$

where BCC shows the index of each BCC.

After finding the minimum amount of unsatisfied demand (TUD^*), a second model is solved that minimizes cost as follows:

$$\begin{aligned}
&min \quad C_H + C_D + C_O + C_C && (4.19)\\
&s.t\\
&C_H = \sum_{p=A+M+1}^{P_m} \left[\sum_{t=A+M+1}^{N-G} (P_H \times F_{p,t}) \right] && (4.20)\\
&C_D = \sum_{p=A+M+1}^{P_m} (P_D \times F_{p,N-G}) && (4.21)\\
&C_O = \sum_{p=1}^{P_m} (P_O \times Z_p) && (4.22)\\
&C_C = \sum_{p=1}^{P_m} (P_C \times W_p) && (4.23)\\
&\sum_{p=1}^{P_m} E_p = TUD^* && (4.24)\\
&(4.2) - (4.18)
\end{aligned}$$

The objective function (4.19) quantifies the total system cost to be minimized. There are 4 cost items: holding cost, disposal cost of blood products, test and separation costs of whole blood (operating cost of laboratory) and delivery cost of collection vehicles per tour. The constraints (4.20), (4.21), (4.22) and (4.23) quantify the related cost items. The constraint (4.24) stands for keeping the total unsatisfied demand at the minimum level (TUD^*) that is found through the solution of the previous model. The rest of the feasible region of this model is identical to the min TUD model.

Note that the min TUD model does not take the system cost into account while investigating minimum level of total unsatisfied demand. Our preliminary computational experiments have shown that solving the min cost model after obtaining the TUD^* value can lead to 95% reduction in the system cost (compared to the cost we obtained in the min TUD model) on average. Hence, using both of these models in a lexicographic optimization approach is necessary to suggest good solutions to the decision makers.

Note that the above formulations include nonlinear terms due to multiplication of decision variables. In the next section we discuss the linear programming based solution approaches to these models.

4.2 Solution Methods

In this section, we present the solution methods that are used to solve the collection and production scheduling problem of thrombocytes under min TUD constraint. By using these methods optimal and near-optimal solutions of the cost minimization model are obtained.

Firstly, a linearization method is implemented to the cost minimization model since it includes some nonlinear terms. (Later on, the linearized model will be used in computational experiments.) Then, a new heuristic approach that couples a customized heuristic algorithm and a simpler version of the linearized cost minimization model is presented.

4.2.1 A Mixed Integer Linear Programming Approach

In this section, we present the corresponding linear programming models (see [29] for more information on this type of linearization involving multiplication of binary and continuous variables and other linearization methods for different cases of nonlinearity).

The nonlinear terms in constraints (4.3), (4.4), (4.5) and (4.6) can be linearized by adding the constraints (4.25), (4.26), (4.27), (4.28), (4.29) and (4.30) into the

models and replacing the multiplications of variables with the new auxiliary decision variables $H_{p,t}(= W_p \times G_{p,t})$ and $D_{p,t}(= Z_p \times X_{p,t})$.
Therefore, the constraints with nonlinear terms will be replaced with (4.31), (4.32), (4.33) and (4.34).

$$-U \times Z_p + D_{p,t} \leq 0 \qquad \forall p \in \{1+A,\dots,P_m\}, t \in \{1+A,\dots,G-M\} \tag{4.25}$$

$$D_{p,t} - X_{p,t} \leq 0 \qquad \forall p \in \{1+A,\dots,P_m\}, t \in \{1+A,\dots,G-M\} \tag{4.26}$$

$$D_{p,t} - X_{p,t} - U \times Z_p \geq U \qquad \forall p \in \{1+A,\dots,P_m\}, t \in \{1+A,\dots,G-M\} \tag{4.27}$$

$$-U \times W_p + H_{p,t} \leq 0 \qquad \forall p \in \{1,\dots,P_m\}, t \in \{1,\dots,G-A-M\} \tag{4.28}$$

$$H_{p,t} - G_{p,t} \leq 0 \qquad \forall p \in \{1,\dots,P_m\}, t \in \{1,\dots,G-A-M\} \tag{4.29}$$

$$H_{p,t} - G_{p,t} - U \times W_p \geq U \qquad \forall p \in \{1,\dots,P_m\}, t \in \{1,\dots,G-A-M\} \tag{4.30}$$

$$G_{p+1,t+1} - G_{p,t} + H_{p,t} = 0 \qquad \forall p \in \{1,\dots,P_m - 1\}, t \in \{1,\dots,G-M-A\} \tag{4.31}$$

$$X_{p+1,t+1} - X_{p,t} - H_{p+1-A,t+1-A} + D_{p,t} = 0 \qquad \forall p \in \{1+A,\dots,P_m - 1\}, t \in \{1+A,\dots,G-M\} \tag{4.32}$$

$$X_{p+A,1+A} - H_{p,1} = 0 \qquad \forall p \in \{1,\dots,P_m - M - A\} \tag{4.33}$$

$$Y_{p+M,t+M} - D_{p,t} = 0 \qquad \forall p \in \{1+A,\dots,P_m - M\}, t \in \{1+A,\dots,G-M\} \tag{4.34}$$

The proof of this linearization technique is provided in the Appendix.

Hence, the linearized model that aims to minimize total cost is as follows:

$$
\begin{aligned}
min \quad & (4.19) \\
s.t \quad & \\
& (4.2) \\
& (4.7) - (4.18) \\
& (4.20) - (4.30) \\
& (4.31) - (4.34)
\end{aligned}
$$

In our preliminary experiments we observed that the linear programming model that minimizes TUD can be solved in negligible time. However, for some real-life problem sizes, the cost minimization model may not be solved in reasonable time, which prompted the use of heuristic approaches for the cost minimization model.

4.2.2 Heuristic Algorithms

In this section, we present four heuristic algorithms that we developed for the cost minimization model. These heuristic methods are created especially for situations when the backorder policy is tight or backorder is not allowed at all. The flowcharts of the heuristic approaches and their explanations are presented below.

The linearized model given in the previous section can be solved in reasonable time for small-sized problem instances. However, this is not the case for real-life problem sizes, at which point heuristic approaches may be necessary.

Computational experiments have shown that attempting to find optimal schedules of both collection and production processes increases problem complexity.

When we keep the collection schedule constant (i.e. when we fix W_ps), the linearized model can find the optimal production schedule within a matter of seconds; the same is true when production schedule is kept constant (i.e. when Z_ps are fixed) and only the collection schedule is determined. However, fixing any one of the two schedules beforehand runs the risk of adversely affecting TUD, which is not acceptable for the purposes of our study.

Therefore, if a schedule that does not violate our policy of keeping TUD at minimum can be derived, such a schedule would render a (heuristic) cost minimization solution possible in reasonable time. The following algorithm outlines the basic approach, which is based on this observation. For the sake of simplicity, when explaining, we will assume that production schedule is fixed first; however as we will explain later, a version in which collection schedule is fixed first, can also be used.

Algorithm 1 General Scheme of the Heuristic Approach

1: Minimize the total amount of unsatisfied demand (TUD) and let the solution be TUD^*
2: Find a production schedule that does not violate the min-TUD policy and fix it.
3: Minimize total cost with the fixed production schedule and keeping TUD at TUD^*. Let the solution be S_1.
4: Fix the collection schedule as in S_1, this time leaving the production schedule as decision. Minimize total cost with the fixed collection schedule while keeping TUD at minimum. Let the solution be S_2.
5: **if** $S_1 = S_2$ **then** declare the result.
6: **else** Fix the production schedule as in S_2 and go back to Step 3.
7: **end if**

In this iterative method, we allow for the model to determine appropriate schedules while keeping total unsatisfied demand at TUD^* and fixing one of the schedules fixed at a time. At each iteration, the model will hopefully approach closer to the optimal result.

To find an initial fixed production schedule in Step 2, two different methods have been devised. The first schedule is a trivial solution in which the production schedule is kept at maximum / full capacity, i.e. production is performed in every period ($Z_p = 1\ \forall p$). Naturally, making production at full capacity does not deviate from min-TUD.

The second method fixes TUD for each period and finds a schedule by calling a *FindSchedule* algorithm, which is designed to determine a schedule that does not violate minimum TUD policy. The *FindSchedule* algorithm is provided below.

Algorithm 2 *FindSchedule Algorithm*

Initialize Z_{last}, W_{prev}, W_{last}, $W_{bfrLastZ}$, W_{count}, a and b as 0. $W_s = 0$ $Z_s = 0$ $\forall s$
$(B^{cum}, T^{cum}) = \mathit{CalCum}\ (B, T, E, p)$
for $p = A + M + 1 \rightarrow P_m$ **do**
    $W_{bfrLastZ} = \mathit{DetAmoInv}\ (Z_{last}, A)$
    $(W_{prev}, W_{last}) = \mathit{DetMaxPosAge}\ (p, W)$
    $(Z, Z_{last}, W_{bfrLastZ}, W, W_{last})$
$= \mathit{TakeDec}\ (B^{cum}, T^{cum}, W_{prev}, B, Z_{last}, W_{last}, Z, A, M, G)$
end for

At the initialization step, variables used in the algorithm are initialized as zero. These variables are: Z_{last} , W_{prev}, W_{last}, $W_{bfrLastZ}$ and W_{count}. When we are at a particular period in the time horizon; Z_{last} stands for the index of the last period that production decision has been taken, similarly W_{last} keeps the index of the period of the last collection decision, W_{prev} records the index of the period of the second last collection decision, $W_{bfrLastZ}$ keeps the period index of the last period that brought whole blood to the RBC before the period of production and W_{count} counts the collection decisions before that particular period.

The functions that we used in *FindSchedule* algorithm are provided below.

Algorithm 3 *CalCum Function* (B, T, E, p)

for $p = 1 \rightarrow P_m$ **do**
    $B_p^{cum} = \sum_{i=1}^{p} B_i$
    $T_p^{cum} = \sum_{i=1}^{p} (T_i - E_i)$
end for

The function *CalCum* calculates the cumulative blood donations collected from the 1^{st} period to the n^{th} period for each period n and similarly calculates the cumulative amount of blood demands that can be satisfied by subtracting the fixed amounts of TUD for each period.

Algorithm 4 *DetAmoInv Function* (Z_{last}, A)

if $Z_{last} - A > 0$ **then**
    for $s = Z_{last} - A \rightarrow 0$ **do**
        if $W_s = 1$ **then**
            $W_{bfrLastZ} = s$
            Break
        end if
    end for
else
    $W_{bfrLastZ} = 0$
end if

The function *DetAmoInv* determines $W_{bfrLastZ}$, index of the last period that collection occurs. We find this index to determine the amount of whole blood that is collected by bloodmobiles and brought to the RBC before the last production. Hence, it determines the amount of blood products in the inventory of RBC.

Algorithm 5 *DetMaxPosAge Function (p,W)*

for $s = p \rightarrow 0$ **do**
    if $W_s = 1$ **then**
        $W_{count} = W_{count} + 1$
        if $W_{count} = 2$ **then**
            $W_{prev} = s$
            Break
        end if
    end if
end for
for $s = p - 1 \rightarrow 0$ **do**
    if $W_s = 1$ **then**
        $W_{last} = s$
        Break
    end if
end for

The function *DetMaxPosAge* determines W_{prev} and W_{last}. These are found in order to determine the maximum possible age of the inventories for both the BCC and RBC at a particular period.

Algorithm 6 *TakeDec Function* $(B^{cum}, T^{cum}, W_{prev}, B, Z_{last}, W_{last}, Z, A, M, G)$

if $\left[T_p^{cum} > B_{W_{bfrLastZ}}^{cum}\right] \,||\, \left[p - (W_{prev} + 1 = G - M) \text{ \& } B_{W_{prev}+1} > 0 \text{ \& } Z_{last} < W_{last} + A\right]$ **then**
    $Z_{p-M} = 1$
    $Z_{last} = -M$
    if $Z_{last} - A > 0$ **then**
        for $S = Z_{last} - A \rightarrow 0$ **do**
            if $W_s = 1$ **then**
                $W_{bfrLastZ} = s$
                Break
            end if
        end for
    else $W_{bfrLastZ} = 0$
    end if
    if $B_{W_{bfrLastZ}}^{cum} < T_p^{cum}$ **then**
        $a = Z_{last} - A$
        $W_a = 1$
        $W_{count} = 0$
        for $s = p - 1 \rightarrow 0$ **do**
            if $W_s = 1$ **then**
                $W_{last} = s$
                Break
            end if
        end for
    end if
    if $a - W_{last} >= G - M - A$ **then**
        $b = G - M - A - W_{last}$
        if $B_{W_{last}}^{cum} >= T_p^{cum}$ **then**
            $W_b = 1$
            $W_a = 0$
        else$W_b = 1$
        end if
    end if
else if $p - W_{last} >= G - M - A$ **then**
    $W_{p-A} = 1$
end if

The function *TakeDec* takes the decisions of production of blood products and collection of whole bloods from BCC to RBC in two cases: If cumulative demand is higher than cumulative blood products inventory then the algorithm determines the last period of production that enables to fulfill the demand and takes a production decision. The algorithm also takes a production decision if there are some whole bloods which must be separated into the blood products because of the bacterial contamination risk that arises at the end of 24 hours. Through this algorithm, we are able to determine a schedule that does not violate minimum TUD policy.

In Figure 4.1, we demonstrate the flowcharts of the two alternative heuristic methods, the first one based on the trivial full production solution and the second one incorporating the algorithm described in the above paragraph.

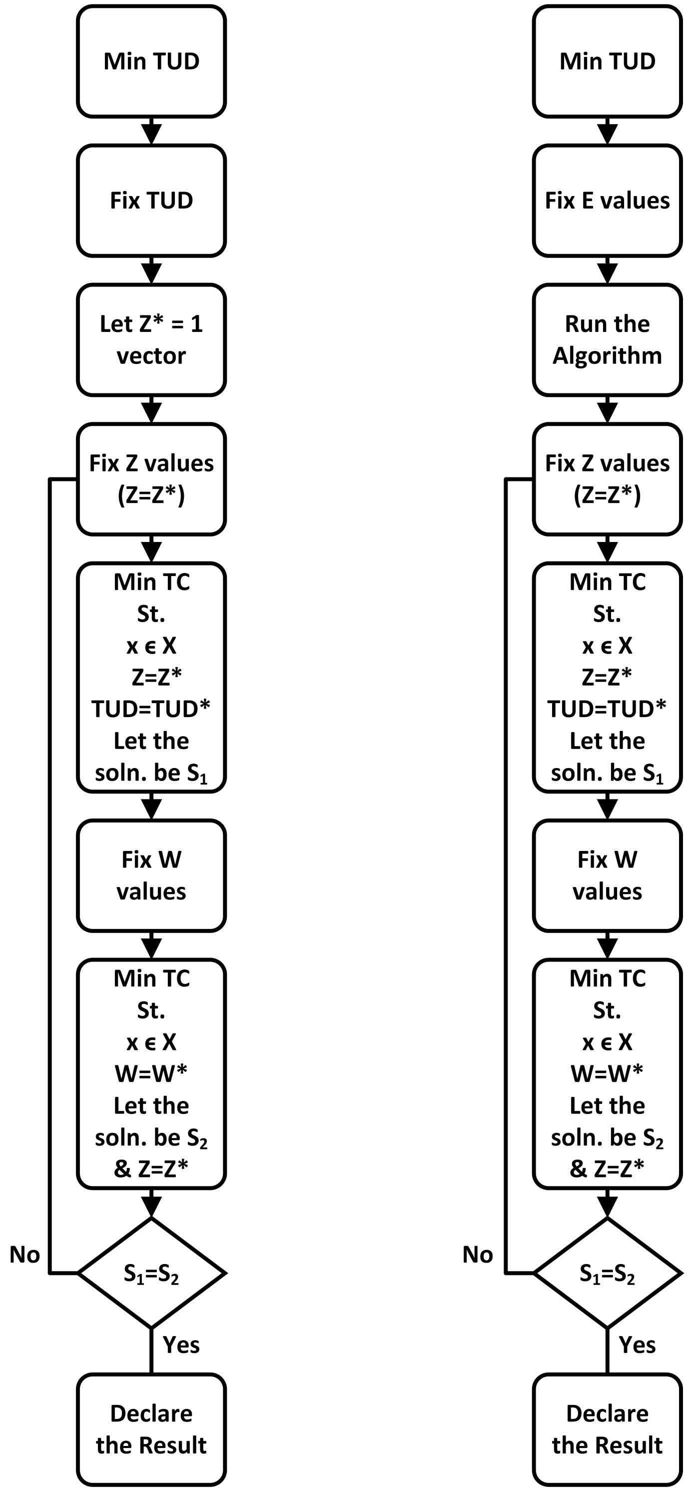

Figure 4.1: Flowcharts of Heuristic Approaches

Recall that, for the sake of simplicity we have explained the heuristic algorithms that first fix the production schedule. It is also possible to modify these algorithms such that collection schedule is fixed first (the two previous methods are modified by just swapping the production and collection terms). This results in four heuristic algorithms: fixing production first-using trivial initial solution, fixing production first-using *FindSchedule* algorithm, fixing collection first-using trivial initial solution, fixing collection first-using *FindSchedule* algorithm. Given that all four heuristics take negligible time to compute, they will be tried consecutively and the one yielding the best result will be chosen.

4.3 Computational Results

We will now provide the results of our computational experiments. We first discuss the data generation method and then present the results of the exact and heuristic solution methods.

4.3.1 Data Generation

In this section, we outline the method used for gathering and generating the problem data used in the computational experiments.

We generated two different sets of problem instances with respect to demand and donation windows. In the first set, we assume that there is a 12-hour demand and donation window, after which the system will remain closed to product orders of hospitals and donations for 12 hours (collection from BCCs, testing and separation activities occur during these remaining twelve hours). In the second set, we assume that demand and donation can occur any time, i.e. the demand/donation window is 24 hours.

The data used in the computational experiments are randomly generated via the random number generator function of Java. In order to observe the system behavior under various settings, different statistical distributions have been used for each of donation and demand parameters. We generated data using uniform distribution and normal distribution (one with relatively small and one with larger variance). The mean values of the distributions are set based on the mean statistic that is provided by the authorities of the TRC. For an average BCC, there are 3 or 4 donations per hour. Therefore, we set the mean value of the normal distributions to 3.5 ($\mu = 3.5$) and define the uniform distribution with the range 0 and 7 in order to abide this mean value. For the normal distribution we tried two different standard deviation parameters to see the effect of increasing variance: 0.875 ($\sigma = 0.875$) and 1.75 (,which is equal to 2σ).

For each couple of donation and demand distributions, five problem instances have been randomly generated. Computational studies was performed for 45 instances in total. The Table 4.1 presents the values that are taken for the other parameters of the cost minimization model (and also for the bi-objective model).

Table 4.1: Values of the Parameters

Parameter	Value	Parameter	Value
P_m	60	G	12
A	3	P_H	0.01334
BO	24 (24-Hour Backorder Policy) 1 (No-Backorder Policy)	P_D	0.0204
M	3	P_O	30
N	60	P_C	30

4.3.2 Computational Results

In this section, we provide the results of the computational studies that we have conducted to evaluate the performance of the cost minimization model and the heuristic approach.

The models and algorithms are coded in JAVA and solved via a dual core

(Intel Core i5-3337U CPU 1.80 GHz) computer with 8 GB RAM. All models are optimized via CPLEX 12.7.1 and the solution times are presented in terms of seconds (real time).

We categorize the results with respect to the combination of donation / demand windows and backorder policies. The considered donation / demand windows are 12 (12H) and 24 (24H) hours. For each of these polices two backorder policies have been discussed: 24-hour backorder limit (any demand must be satisfied in 24 hours after the time of ordering, otherwise it will be lost) and no-backorder. This yields four separate sets of computational studies.

Tables 4.2, 4.3, 4.4 and 4.5 contain the solution times of the cost minimization model for each couple of donation/demand distributions.

Table 4.2: Computational Results for 12H-Window Under 24-Hour Backorder Policy

Statistical Distribution		Solution Time (sec)	
Donation	Demand	Average	Max
U	U	5.94	28.28
	$N(\mu,(\sigma)^2)$	7.15	18.34
	$N(\mu,(2\sigma)^2)$	6.67	28.20
$N(\mu,(\sigma)^2)$	U	6.80	34.34
	$N(\mu,(\sigma)^2)$	2.51	16.31
	$N(\mu,(2\sigma)^2)$	3.58	19.27
$N(\mu,(2\sigma)^2)$	U	9.07	39.95
	$N(\mu,(\sigma)^2)$	9.95	52.56
	$N(\mu,(2\sigma)^2)$	8.12	54.59

When the time window is 12 hours and the backorder limit is 24 hours, the computational studies have shown that the cost minimization model can be solved optimally for all problem instances that have been generated (Table 4.2). The solution times are all under a minute, which shows that it can be used in daily decisions of blood band services of TRC. Note that, currently the TRC operates the labs 24 hours a day. In the computational results, it is seen that in optimal solutions lab works 10 hours on average. This shows that by using this modeling approach it is possible to reduce the operating costs of labs about 60%. Also note that, this setting is the closest one to the current setting of TRC. However, other settings may also be relevant in other blood bank systems around the world. Table 4.3 presents the computational results of a system with 24H-Window and 24-hour backorder policies. It is seen that optimal solutions have been obtained under an hour, which is half of a period.

Table 4.3: Computational Results for 24H-Window Under 24-Hour Backorder Policy

Statistical Distribution		Solution Time (sec)	
Donation	Demand	Average	Max
U	U	322.42	3436.56
	$N(\mu,(\sigma)^2)$	238.69	1270.31
	$N(\mu,(2\sigma)^2)$	292.90	2009.27
$N(\mu,(\sigma)^2)$	U	99.68	225.88
	$N(\mu,(\sigma)^2)$	149.41	477.89
	$N(\mu,(2\sigma)^2)$	113.72	589.00
$N(\mu,(2\sigma)^2)$	U	80.08	198.34
	$N(\mu,(\sigma)^2)$	118.76	404.31
	$N(\mu,(2\sigma)^2)$	106.76	363.14

Computational studies were also conducted for a system where any demand that cannot be satisfied at the period of ordering is lost. The results are presented in the following tables.

Table 4.4: Computational Results for 12H-Window Under No-Backorder Policy

Statistical Distribution		Solution Time (sec)	
Donation	Demand	Average	Max
U	U	14.03	14.56
	$N(\mu,(\sigma)^2)$	14.43	16.34
	$N(\mu,(2\sigma)^2)$	14.57	16.75
$N(\mu,(\sigma)^2)$	U	14.20	15.34
	$N(\mu,(\sigma)^2)$	13.56	14.05
	$N(\mu,(2\sigma)^2)$	14.13	15.03
$N(\mu,(2\sigma)^2)$	U	14.04	15.08
	$N(\mu,(\sigma)^2)$	14.66	17.23
	$N(\mu,(2\sigma)^2)$	13.95	15.36

Table 4.4 shows that even under no-backorder policy the linearized model is able to find the optimal solutions of any data set while 12H-Window is assumed for demand orders and donations. Although the solution times have increased, the performance of the model is still suitable for real-life problems.

The last computational study that we have conducted to evaluate the linearized MIP approach is performed on a system where 24H-Window and no-backorder policies are used together. Table 4.5 shows that for this type of a blood bank system, optimal solution of the problem can not be found under the time limit of 3600 seconds. Although, the optimality gaps are low (around 1%), the solution times are quite high for a decision support tool that will be used daily decisions of a blood bank.

Table 4.5: Computational Results for 24H-Window Under No-Backorder Policy

Statistical Distribution		Solution Time (sec)		Optimality Gap (%)	
Donation	Demand	Average	Max	Average	Max
U	U	2434.61	3600.00	0.38%	1.00%
	$N(\mu,(\sigma)^2)$	2098.72	3600.00	0.26%	0.94%
	$N(\mu,(2\sigma)^2)$	3010.87	3600.00	0.49%	1.24%
$N(\mu,(\sigma)^2)$	U	2513.84	3600.00	0.35%	0.73%
	$N(\mu,(\sigma)^2)$	141.89	435.31	0.00%	0.00%
	$N(\mu,(2\sigma)^2)$	3404.10	3600.00	0.45%	0.57%
$N(\mu,(2\sigma)^2)$	U	3600.00	3600.00	0.35%	0.59%
	$N(\mu,(\sigma)^2)$	1641.81	3600.00	0.42%	1.05%
	$N(\mu,(2\sigma)^2)$	2906.25	3600.00	0.60%	0.94%

These results show that under 12H-Window policy, the cost minimization model is suitable to be used for real-life problems of blood bank systems with any backorder limit policies. However, the problem becomes complicated when the demand and donation can occur any time and no backorder is allowed. The heuristic algorithms mentioned in the previous section have been used in order to find good quality solutions for these problems. Table 4.6 summarizes the computational results of these algorithms. We have tried all four versions of the heuristic algorithms and taken the best solution as the overall heuristic solution.

Table 4.6: Computational Results Heuristic Approach on a System with 24H-Window and No-Backorder Policies

Statistical Distribution		Solution Time (sec)		Gap w.r.t the Best Solution (%)	
Donation	Demand	Average	Max	Average	Max
U	U	103.12	173.00	3.05%	6.87%
	$N(\mu,(\sigma)^2)$	102.38	130.17	2.58%	5.98%
	$N(\mu,(2\sigma)^2)$	111.05	149.31	3.94%	8.11%
$N(\mu,(\sigma)^2)$	U	128.01	169.66	1.37%	3.10%
	$N(\mu,(\sigma)^2)$	91.22	112.36	1.23%	3.09%
	$N(\mu,(2\sigma)^2)$	93.94	117.49	2.33%	7.56%
$N(\mu,(2\sigma)^2)$	U	75.71	126.90	2.11%	4.54%
	$N(\mu,(\sigma)^2)$	86.13	106.27	1.02%	2.40%
	$N(\mu,(2\sigma)^2)$	123.29	160.08	1.85%	4.18%

As it can be seen in the above table, developed heuristic algorithms are able to find good quality solutions for the problems in reasonable time. The average solution time has decreased from 2416.9 seconds to 101.65 seconds. The heuristic approach was able to find the optimal solution in 7 of the 45 problem instances. The average gap with respect to the best solution is only 2.16%, while for only 5 of the instances, the heuristic solution has a gap above 5%. These results show that, in order to shorten the solution time, the heuristic algorithms can be used for real-life problems.

Chapter 5

A Bi-Objective Extension

In this chapter, a bi-objective extension for the whole blood collection and thrombocyte production scheduling problem of regional blood centers is presented.

We first introduce an additional objective, maximizing quality of thrombocyte and the motivation behind using this objective. We then provide the related bi-objective mixed integer linear programming model and explain the solution approach, the $\mathcal{E}$-Constraint Method, that is used to find the Pareto-optimal/efficient solutions of the model. We demonstrate the trade-off between the two objective functions, maximizing quality of thrombocyte and minimizing the total cost of the system, by a sample Pareto-chart. We finally present the results of our computational experiments. These results show that considering both objectives may improve the decision making process and lead the decision maker to a better system performance.

5.1 Mathematical Models

Cost minimization is an important objective that has to be considered in any system with finite resources. However, another objective that the TRC attaches importance to is quality maximization. In the meetings that we held with the

TRC authorities, it is stated that the age of whole blood at the time of separation into blood products directly affects the quality of these products. In other words, the younger whole blood is separated out, the higher quality product is rendered.

We developed a new age-based function, which is a weighted aggregation of newly produced thrombocyte amount, where the weights are proportional to the age of the product. By minimizing this function (5.1), we aim to reduce the overall age of newly produced thrombocyte. The resulting model is based on the same feasible region as our previous cost minimization model and is as follows:

$$min \quad \sum_{p=A+M+1}^{P_m} \sum_{t=A+M+1}^{G} t \times Y_{p,t} \tag{5.1}$$

$$s.t$$

$$(4.2)$$

$$(4.7) - (4.18)$$

$$(4.20) - (4.34)$$

The objective function (5.1) penalizes each unit of newly produced blood product proportional to its age (measured in number of periods) at the time of entering the inventory. This bi-objective modeling approach aims to help the decision makers to observe the relation between cost and quality and choose their preferred solution from a set of Pareto solutions.

In the next section, we explain the $\mathcal{E}$-Constraint Method, which is the solution approach chosen to conduct the bi-objective study of cost minimization and quality maximization objectives.

5.2 Solution Approach: The $\mathcal{E}$-Constraint Method

The $\mathcal{E}$-Constraint Method is a solution approach for multi-objective optimization problems (MOP) and may be used in order to find the pareto-optimal/efficient solutions for these problems. In the following, we present brief explanations of the MOP and this method. After that, we demonstrate its implementation on our collection and production scheduling problem.

A multi-objective programming problem with K objectives can be formulated as follows:

$$\begin{array}{ll} \textit{min (max)} & z(x) = (z_1(x), z_2(x), \ldots, z_K(x)) \\ \textit{subject to} & x \in X \end{array}$$

where, x is the decision variable vector, X be the feasible region, Z is the set of objective value vectors of the feasible decision vectors. Z is the image of the feasible decision space (X) in the criteria space.

For the most part, a trade-off relationship is observed between the objectives; hence, no single solution optimizes all objective functions. Otherwise, the problem is not a multi-criteria decision making problem already. Therefore in these problems, we put the concepts *non-dominance* and *efficiency* in the place of *optimality* [30]. When dealing with this kind of problems, *non-dominated/efficient* solutions are the focus of interest rather than a single optimal solution.

A vector y is dominated by another vector x, if x is at least as good as y on all criteria while being strictly better for at least one criterion ([30]). A *non-dominated* solution is an objective function vector which is not dominated by any other objective function vector in the feasible criteria set and therefore it has a potential to be the best solution for a decision maker. If a objective function vector $z(x)$ is non-dominated, the corresponding decision variable vector x is *efficient*. The aim of the solution approaches that are developed for multiple criteria decision problems is to find the non-dominated solutions [30].

In this study, the $\mathcal{E}$-Constraint Method (lexicographic version) is used to find the efficient solutions of the bi-objective model that we define. The main idea of the $\mathcal{E}$-Constraint Method is optimizing one of the K objective functions while limiting the others by assigning a constraint for each of them. The generic scalarization model solved in this approach is provided below:

$$
\begin{array}{lll}
\textit{min (max)} & Z_k(x) & \\
\textit{subject to} & Z_m(x) \geq \epsilon_m & \forall m \in M, \quad m \neq k \\
 & Z_n(x) \leq \epsilon_n & \forall n \in N, \quad n \neq k \\
 & x \in X &
\end{array}
$$

, where M is the set of objective functions that are to be maximized and N is the set of objective functions that are to be minimized. By solving such single objective scalarization models iteratively and making systematic changes in ϵ_m and ϵ_n values, the set of non-dominated solutions can be obtained.

Let us consider a bi-objective problem (a multi-objective problem with two objectives) with the objective functions z_1 and z_2 where both are to be minimized. The $\mathcal{E}$-Constraint Method is based on iteratively solving the following two models:

$$
\begin{array}{ll}
\min z_1(x) & \qquad \min z_2(x) \\
s.t.\ \ z_2(x) \leq \epsilon_2 & \qquad s.t.\ \ z_1(x) = \epsilon_1 \\
\quad x \in X & \qquad \quad x \in X
\end{array}
$$

The steps of the lexicographic approach are as follows: First, run the model on the left (let it be P_1) with a big M value for ϵ_2. Set ϵ_1 to the optimal objective value (let it be z_1^*) of P_1. Then, solve the second model (let it be P_2) under the constraint with $\epsilon_1 = z_1^*$. Through this approach, the first model finds the optimal solution that minimizes z_1 and the second model finds the best level of z_2 for this specific level of z_1. Let the optimal solution of P_2 be (z_1^*, z_2^*). (z_1^*, z_2^*) is a non-dominated solution for the bi-objective model. By setting the ϵ_2 value to $z_2^* + \Delta$, where Δ is a predetermined stepsize, and solving these two models iteratively, the next non-dominated solution can be found. The steps of this procedure are presented in Algorithm 7.

Algorithm 7 The Procedure of Lexicographic $\mathcal{E}$-Constraint Method for a Bi-Objective Problem

1: Δ=1. $\epsilon_2 = M$ (M is a big enough number). $PS = \emptyset$ (The set of Pareto solutions).
2: Optimize P_1.
3: **if** P_1 is infeasible **then** Stop the procedure!
4: **else** Let z_1^* be the optimal objective value of P_1, $\epsilon_1 = z_1^*$.
5: **end if**
6: Solve P_2 and let z_2^* be the optimal objective value of P_2
7: $PS = PS \cup (z_1^*, z_2^*)$
8: $\epsilon_2 = z_2^* + \Delta$
9: Go back to Step 2

In the bi-objective framework with cost minimization and quality maximization objectives, the cost minimization model that is presented in Chapter 4 corresponds to model P_1 and the quality maximization model which is introduced in Chapter 5 is model P_2 with an additional constraint on the total cost value. Since the objective values of the quality maximization model are all integers, we can obtain the whole set of non-dominated solutions by setting the stepsize value Δ to 1.

In the next section, the summary of computational results of the bi-objective study and a sample Pareto-chart, which demonstrates the trade-off relationship between the two objectives, are presented.

5.3 Computational Results

In our computational experiments we have used the randomly generated data created for the cost minimization setting with $\mu = 3.5$ and $\sigma = 0.875$ (discussed in Chapter 4). The parameters are taken the same as in the previous chapter except the P_m, A, M, N and G.

For the computational experiments of bi-objective extension of the problem the time horizon is still 5 days but each period in the model is equal to 6 hours. Hence, there are 20 periods in these models ($P_m = 20$). This size reduction has been made in order to not exceed the RAM capacity of the computer that we have used for these computational studies. Since, the number of periods has been reduced, we have also modified the values of A, M, N and G in order to have the same values for the parameters in terms of hours (real time). They all reduce to one third of the values that are presented in the previous chapter.

We first provide a sample Pareto chart for one example instance in Figure 5.1. The chart demonstrates the trade-off between the cost and quality criteria. Increasing quality (having younger products) increases the total system cost since the collection and production activities have to be performed more frequently. It is also observed that the relation between these two criteria is not linear, due to the structure of the feasible set (non-convex).

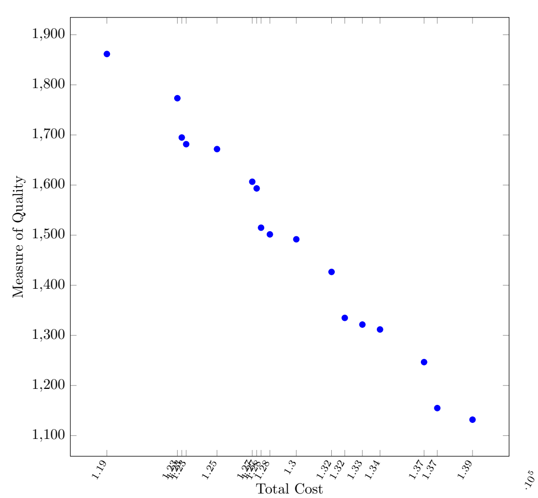

Figure 5.1: Sample Pareto-Chart for Min Cost - Max Quality Objectives

The summary of the results for each type of data set are shown in Tables 5.1 and 5.2. In these tables, the average and maximum values for the number of non-dominated solutions and solution times are presented over the five randomly generated instances of 24 hour backorder settings.

Table 5.1: Computational Results of the Bi-Objective Problem under 12H-Window and 24-Hour Backorder Policies

Statistical Distribution		Solution Time (sec)		# of Non-dominated Solutions	
Donation	Demand	Average	Max	Average	Max
U	U	2.20	3.24	12.60	23
	$N(\mu,(\sigma)^2)$	1.60	2.22	9.80	17
	$N(\mu,(2\sigma)^2)$	1.40	2.06	8.60	11
$N(\mu,(\sigma)^2)$	U	1.40	2.19	8.60	11
	$N(\mu,(\sigma)^2)$	1.20	1.76	7.40	11
	$N(\mu,(2\sigma)^2)$	1.60	2.54	7.40	11
$N(\mu,(2\sigma)^2)$	U	1.40	2.41	10.20	14
	$N(\mu,(\sigma)^2)$	1.60	2.35	9.00	15
	$N(\mu,(2\sigma)^2)$	1.40	2.26	8.40	13

Table 5.2: Computational Results of the Bi-Objective Problem under 24H-Window and 24-Hour Backorder Policies

Statistical Distribution		Solution Time (sec)		# of Non-dominated Solutions	
Donation	Demand	Average	Max	Average	Max
U	U	12.20	17.94	38.00	89
	$N(\mu,(\sigma)^2)$	22.40	36.13	53.20	83
	$N(\mu,(2\sigma)^2)$	22.20	38.28	57.00	92
$N(\mu,(\sigma)^2)$	U	12.20	19.18	30.60	75
	$N(\mu,(\sigma)^2)$	24.20	33.61	49.00	81
	$N(\mu,(2\sigma)^2)$	15.60	26.90	42.60	63
$N(\mu,(2\sigma)^2)$	U	12.20	26.52	36.00	96
	$N(\mu,(\sigma)^2)$	18.00	28.85	45.20	68
	$N(\mu,(2\sigma)^2)$	26.60	34.28	51.80	79

Chapter 6

Conclusion

Motivated by the real life applications in the Turkish Red Crescent (TRC); we propose a mathematical modeling approach for managing blood bank operations. The underlying problem is challenging due to a number of factors. First, the relevant "goods" (whole blood and blood products) are highly perishable and become completely unusable after a given number of days following donation, a result that must be avoided as much as possible, given the fact that the supply often fails to meet demand. The second factor is that cost minimization of a blood services system cannot be the primary concern. Blood products are utilized for a variety of life threatening situations, hence one should not compromise from maximum demand satisfaction. The proposed approach is built on these premises and addresses the following:

We first describe the current system of the Turkish Red Crescent and provide an extensive literature review for other relevant works that also deal with optimizing blood product services. Unlike the other studies in the literature that focus on collection, ordering or production decisions separately, we develop an approach that handles both collection and production decisions simultaneously. The fourth chapter presents the proposed model for cost minimization, while the fifth chapter introduces into that same model, the concern of quality maximization alongside cost minimization, resulting in a bi-objective programming model.

In our proposed model under Chapter 4, we dealt with the cost minimization setting. We first presented our first model that minimizes the total unsatisfied demand (TUD) for thrombocyte suspension (TS). The second model minimizes the total cost while ensuring that the TUD is at the minimum level possible. These two models constitute a single lexicographic bi-objective model. We investigate various exact and heuristic approaches to find optimal and heuristic solutions to these models. While it is possible to find the optimal solution of this model in small size problem instances, real life problem sizes may not allow for timely calculation of optimal solutions. Therefore, we develop novel heuristic algorithms. Our computational tests show the satisfactory behavior of these algorithms.

The bi-objective mixed integer linear programming model with cost minimization and quality maximization objectives is solved with the $\mathcal{E}$-Constraint Method. The results of our computational experiments show that considering both objectives may improve the decision making process and lead the decision maker to a better system performance.

This study can be extended in a number of ways. The current study assumes a deterministic environment. A stochastic extension, taking the stochasticity in demand and donation can be considered. In related literature, most of the stochastic studies are conducted by using Two-Phase Stochastic Programming approach. The same approach can also be adapted for our problem setting.

The bi-objective extension that we proposed was demonstrated on small-size problem instances due to computational restrictions. Future research can be conducted on developing computationally efficient exact solution algorithms that can tackle real-life problem sizes.

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Appendix

Proof of the linearization method that we used in Chapter 4 is presented below:

Statement. Let $x_1 \in \{0, 1\}$ be a binary variable and x_2 and y be continuous variables such that $0 \leq x_2 \leq u$, where u is some positive real number. If the following inequalities are satisfied,

$$y \leq ux_1$$
$$y \leq x_2$$
$$y \geq x_2 - u(1 - x_1)$$
$$y \geq 0$$

then $y = x_1 x_2$

Proof. Assume that the binary variable x_1 is equal to 0. Under this assumption, the constraints can be reorganized as follows:

$$y \leq 0$$
$$y \leq x_2$$
$$y \geq x_2 - u$$
$$y \geq 0$$

The first and the fourth constraints imply that $y = x_1 x_2 = 0$. The other constraints are trivially satisfied.

When x_1 is equal to 1, the constraints can be reorganized as follows:

$$y \leq u$$
$$y \leq x_2$$
$$y \geq x_2$$
$$y \geq 0$$

The second and the third constraints imply that $y = x_1x_2 = x_2$. The other constraints are trivially satisfied.

By examining all possible situations it is validated that the provided set of constraints force the variable y to take the value of x_1x_2.

□