# ANALYZING SUPPLY CHAIN NETWORKS FOR BLOOD PRODUCTS

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## ABSTRACT

The blood supply chain, starting from the donor until the blood is used to meet transfusion demands of patients, is a multi-echelon and complex system. The perishable and lifesaving characteristics of blood products, such as red blood cells and platelets, as well as uncertainties in both supply and demand make it difficult to maintain a balance between shortage and wastage due to expiry. An effective blood supply chain should be able to meet the demand while at the same time reducing wastage and total operational cost. In order to be cost effective, the related organizations have to decide how much blood should be collected from donors, how much blood products should be produced at the blood center, and how much blood products should be distributed to hospitals or transshipped between hospitals.

The objective of this dissertation is to provide these tactical and operational decisions to guide those who work in healthcare supply chain management and explore new opportunities on performance improvement for an integrated blood supply chain by optimization with aim of minimizing total cost, consideration of transshipment between hospitals, and application of a coordinated multi-product model.

This dissertation presents three multi-stage stochastic models for an integrated blood supply chain to minimize total cost incurred in the collection, production, inventory, and distribution echelons under centralized control. The scope of this study focuses on modeling a supply chain of blood products in one regional blood center, several hospitals and blood collection facilities. First, we develop an integrated model for the platelet supply chain that accounts for demand uncertainty and blood age information, then we develop this model further by investigating the impact of transshipment between hospitals on cost savings, and then we propose a multi-product model that accounts for red blood cells and platelets at the same time

and compare it with an uncoordinated model where the red blood cell and platelet supply chains are considered separately.

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## DEDICATION

This dissertation is dedicated to my father, mother, uncle, sister, and brother for their unconditional love and endless support.

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# CHAPTER 1. INTRODUCTION

## 1.1. Background

### 1.1.1. Blood products

Blood is an essential body fluid in humans that delivers oxygen and nutrients to the cells and gets rid of carbon dioxide, ammonia, and other waste products. There are more than 4,000 different kinds of components in blood (Beliën & Forcé, 2012). We distinguish the following four most important types of blood products: whole blood, red blood cells (RBC), plasma (PLS) and platelet (PLT). Table 1 summarizes the color, shelf life, storage requirement, and key medical uses of these blood products (American Red Cross, 2017a). Whole blood is the most popular blood donation type, but it is now rarely used for transfusion. This is because most patients only require a specific element of blood, such as red blood cells or platelets, and a single component dose is more effective. Therefore, collected whole blood units are usually separated into several components via centrifugation in order to meet transfusion demands.

Red blood cells are the most abundant cell type and normally make up 40-50% of whole blood volume. They are mainly used to deliver oxygen to body cells and transport carbon dioxide to the lungs. As the most demanded blood product, red blood cells is perishable and can only be stored for 42 days at low temperatures (American Red Cross, 2017a). Plasma is the liquid portion of blood and is composed of protein, sugar, fat and salt solution. It plays a variety of roles including clotting, defense and transport. Plasma is the only blood component that is not perishable and it has a shelf life of 1 year (American Red Cross, 2017a). Platelets are the small colorless cell fragments in blood and are mainly used to stop bleeding. They are useful in cancer treatment, organ transplants, and general surgeries. Platelets are highly perishable and can only be stored for 5 days (American Red Cross, 2017a).

**Table 1. Summary of blood products**

| Blood Products | Color | Shelf Life | Storage | Key Uses |
|---|---|---|---|---|
| **Whole Blood** | Red | 21/35 Days | Refrigerated (+2℃ to +6℃) | Trauma, Surgery |
| **RBC** | Red | 42 Days | Refrigerated (+2℃ to +6℃) | Trauma, Surgery, Anemia, Blood loss and disorders |
| **PLS** | Yellowish | 1 Year | Frozen (-25℃ or colder) | Burn patients, Shock, Bleeding disorders |
| **PLT** | Colorless | 5 Days | Room temperature with agitation (+20℃ to +24℃) | Cancer treatment, Organ transplants, Surgery |

Blood types depend on the presence or absence of two antigens, A and B, and a protein rhesus factor. There are eight main blood types: A, B, AB and O, each of which can be rhesus positive or negative. Figure 1 shows the distribution of blood types in the US blood donor population (AABB, 2017). O+ takes the largest proportion and A+ the second. Crossmatching of blood types is important for safe transfusions, especially for red blood cells as not all blood types are compatible. While it is not necessary to consider crossmatching for platelets.

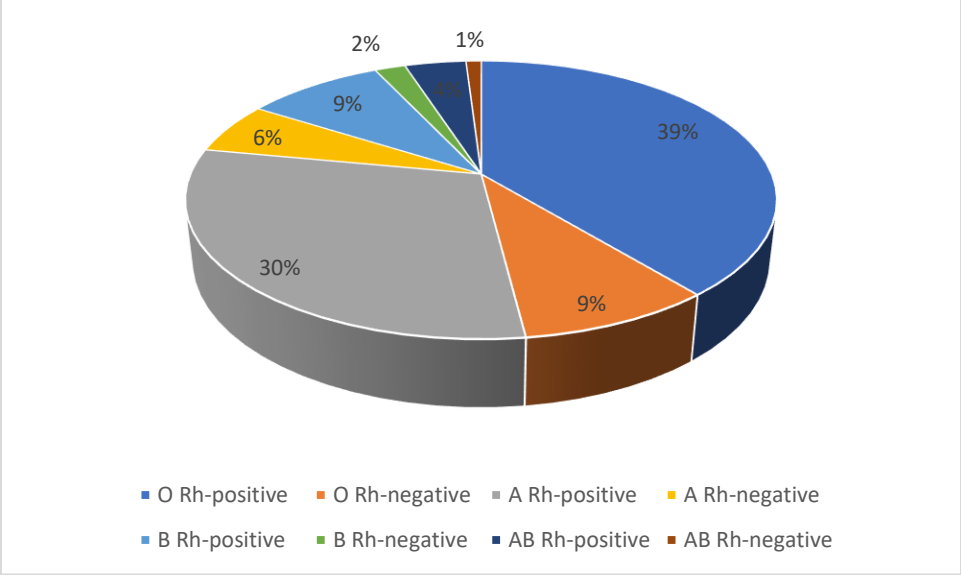


**Figure 1. Distribution of blood types in the US blood donor population**

### 1.1.2. Blood supply chain

The supply chain for blood and its components (i.e. red blood cells, plasma, and platelets) starts with donors and ends with patients. As depicted in Figure 2, the blood supply chain generally consists of four main echelons: collection, production, inventory, and distribution. (Osorio et al., 2015).

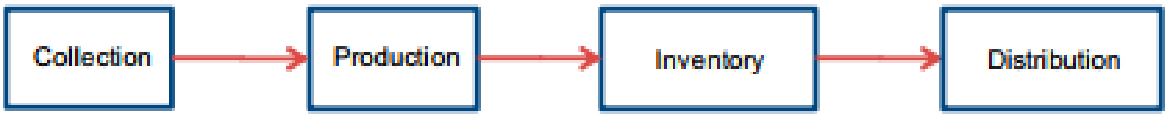


**Figure 2. Echelons of the blood supply chain**

The blood supply chain starts with the collection of blood from donor populations. Blood can be donated at three different facilities: bloodmobiles, blood centers, and hospitals. A bloodmobile is a large vehicle (usually a bus or a large van) equipped with necessary equipment for blood donation. It usually travels to public places with a high population density, such as colleges and churches, to collect blood. As a temporary blood collection facility, the bloodmobile normally only collects whole blood. These donated whole blood units should be transferred to blood centers and processed within six hours in order to extract platelets (Mobasher et al., 2015).

The most common blood donation type is whole blood. A whole blood donation usually takes about 10 to 20 minutes. About 1 pint of blood and several small test tubes are collected from a donor. Apart from donating whole blood, donors can donate a single blood component with the help of an apheresis machine. Apheresis is the process of collecting a specific component of the blood, such as red blood cells or platelets, and returning the remaining components back to the donor. Although this process takes longer than that of whole blood donation, approximately one to two hours, it collects more units of one particular component of blood than could be separated from a unit of whole blood. For example, the number of platelets

collected from one apheresis donation would normally equal to up to four to six times that from one whole blood donation (American Red Cross, 2017b).

In the production echelon, most of the blood from a donor is spun in centrifuges to separate it into red blood cells, platelets, and plasma. At the same time, the test tubes from the same donor will be sent to a testing laboratory to perform tests for infectious diseases such as HIV, HBV, and HCV. If any test has a positive result, the blood units will be discarded. It usually takes about two days for the processing and testing of whole blood, while only one day is needed for testing of apheresis derived blood products.

After completing the processing and testing procedures, blood units that are suitable for transfusion are put into inventory. Maintaining an appropriate level of inventory is very important. However, the perishable characteristic of blood products, demand uncertainty, together with the crossmatching of ABO blood types, increases the complexity for making inventory decisions.

The distribution process mainly refers to the transport of blood products from a regional blood center to different hospitals. In addition, blood can also be transshipped from one blood center to another blood center or from one hospital to another hospital. The internal transfer of blood products from a hospital blood bank to the transfusion point is also possible.

### 1.2. Problem statement

Compared to a traditional supply chain, the blood supply chain has several special characteristics. Firstly, blood is an indispensable component of human life and shortages can cause serious consequences such as the loss of human life. Secondly, blood is a scarce resource and can only come from human donations. Thirdly, blood products such as platelets and red blood cells are highly perishable which can lead to a lot of waste due to expiration without

effective management of the supply chain. Balancing the shortage and wastage is extremely hard for the blood supply chain because of these characteristics as well as unpredicted supply and demand. The crossmatching of blood types for red blood cells adds more complexity to decision makers in healthcare supply chain management. It is necessary to develop an effective blood supply chain that meets the transfusion demand while at the same time reducing wastage and total operational cost.

Therefore, the study investigates the integrated blood supply chain and explores opportunities to minimize total cost incurred during the collection, production, inventory, and distribution echelons under centralized control. In a centralized control system, centralized replenishment/production decisions are made for all participants of the supply chain to directly minimize the system-wide operational cost instead of minimizing individual operational cost for each participant independently. This represents a socially optimal supply chain model. Based on the process of the blood supply chain, we consider production cost, holding cost, shortage cost, outdating cost and transportation cost when calculating the total operational cost.

Even though there are four types of transfusable products that can be derived from blood: red blood cells, platelets, plasma and cryoprecipitate, most papers about blood supply chain management deal with platelets or red blood cells since the other two products are nonperishable products and can be used for up to one year after collection. Handling supply chain management of plasma and cryoprecipitate is significantly less complex than platelets and red blood cells. In addition, red blood cells and platelets are in high demand every day in the US. Therefore, this research focuses on modeling the supply chain management of red blood cells and platelets.

Platelets, as the most perishable blood product, are less explored by researchers regardless of their critical medical importance. This may be due to the difficulty of maintaining a

balance between wastage and shortage for platelets. Intrigued by a BloodMove Platelets project conducted throughout regional South Australia where a significant reduction in platelet wastage due to expiry was attained by transshipment between hospitals (National Blood Authority, 2016), we consider transshipment as a good way to optimize the supply chain management of platelets. Compared to platelets, red blood cells have a much longer shelf life. As whole blood can be separated into red blood cells, platelets, and other nonperishable blood components, considering multiple products is necessary for accurate modeling of supply and demand.

In this study, we develop three stochastic models for an integrated blood supply chain to minimize total cost incurred during the collection, production, inventory, and distribution echelons under centralized control. First, we present a stochastic model for the platelet supply chain that accounts for demand uncertainty and stock age information, then we develop this model further by investigating the impact of transshipment between hospitals on cost savings, and then we propose a multi-product model that accounts for red blood cells and platelets at the same time and compare it with an uncoordinated model where the red blood cell and platelet supply chains are considered separately.

## 1.3. Significance of the study

In this section, we present contributions of this study to the blood supply chain literature. In addition, we provide several managerial insights to guide those who work in healthcare supply chain management.

### 1.3.1. Platelet supply chain

This study develops a novel multi-stage stochastic optimization model for an integrated platelet supply chain that accounts for demand uncertainty and blood age information. Apheresis and whole blood collection are both incorporated into the mathematical model. Three types of

patients have been categorized for platelet demand in different age range. This study has several research contributions. First, this research is the first study in the blood supply chain literature that models demand uncertainties using a multi-stage stochastic program with a daily stage length. A multi-stage stochastic program performs better than a two-stage program in reflecting and representing demand uncertainties for a multi-period system. Second, we observed that it is not necessary for researchers to enforce constraints regarding following a FIFO issuing policy to achieve an optimal performance when optimizing the platelet supply chain. Finally, we found that recruiting more donors at hospitals and maintaining a minimum capacity level of 60 units at the blood center could lead to performance improvement for the platelet supply chain. The details of this study are shown in Chapter 2.

### 1.3.2. Platelet supply chain considering transshipment

A few researchers have observed that transshipment or collaboration brought significant reduction in outdate and shortage rates in blood supply chain management. However, we are unaware of any study that incorporates transshipment into a mathematical model to measure the specific impact of transshipment on wastage and total operational cost. Therefore, the main contribution of this study is that we present the first multi-stage stochastic program for an integrated platelet supply chain considering transshipment, demand uncertainty, and age information and investigates the benefit of transshipments on reducing total cost and shortage. The details of this study are shown in Chapter 3.

### 1.3.3. Multi-product supply chain

Most literature regarding blood supply chain management talks about a single blood product such as red blood cells or platelets, we are unaware of any study that discusses an integrated blood supply chain which takes multiple blood products and multiple production

processes into account. As donated whole blood can be separated into red blood cells, platelets and plasma, considering multiple products is necessary for coordinating different types of production processes and maintaining an appropriate inventory level. Therefore, the main contribution of this study is that we present the first multi-product multi-period stochastic program for integrated blood supply chain that accounts for demand uncertainty, age information, blood type substitution, and demand types for platelets. Besides, the proposed multi-product model is compared with an uncoordinated model where the red blood cell and platelet supply chains are considered separately under different scenarios of donors. The details of this study are shown in Chapter 4.

### 1.3.4. Managerial insights

It is important for administrators and decision makers to make optimal tactical and operational decisions on collection, production, inventory, and distribution of blood products that account for cost efficiency along with controlling shortage and wastage. Therefore, we provide the following managerial insights:

- It is possible to optimize platelet production, storage, and distribution on a daily basis. The feasibility of this optimization renders the use of heuristic rules, such as FIFO issuing policies, unnecessary.
- Recruiting more donors at hospitals is a promising strategy to reduce total operational cost, especially shortage cost. Maintaining enough storage capacity at the blood center is an effective approach to control shortage.
- Transshipment is an effective strategy to save total cost along with reducing shortage and wastage for the platelet supply chain. We encourage hospitals to build mutual trust and share stock information to allow transshipment of platelets.

- When a limited donor base is available at hospitals, implementing transshipment between hospitals can be an effective alternative to recruiting more donors to reduce shortages. Though implementing transshipment is not a trivial task, increasing the number of donors is also challenging, as evidenced by the low level of participation among potential donors.
- When storage capacity for platelets at blood centers is limited, implementing transshipment between hospitals can be an effective alternative to increasing storage capacity to reduce shortages. Though implementing transshipment is not a trivial task, increasing storage capacity of platelets is also challenging as they must be agitated gently and continuously at controlled temperatures.
- Coordinating supply chains for red blood cells and platelets at the same time can save a lot of cost, especially when making decisions on blood collection and production. Managers should stop focusing on one single blood product while ignoring the fact that red blood cells and platelets share the same production process.
- It is more necessary to coordinate the red blood cell and platelet supply chains if the number of available donors is sufficient because more cost savings can be attained in this situation. This is particularly true when apheresis donors take a large proportion.
- It is more cost effective to apply whole blood donation compared to apheresis donation. However, the percentage of each type of blood donation also depends on the demand differences between red blood cells and platelets.

# CHAPTER 2. A MULTI-STAGE STOCHASTIC OPTIMIZATION MODEL FOR INTEGRATED PLATELET SUPPLY CHAIN

## 2.1. Abstract

This study presents a multi-stage stochastic program for a platelet supply chain with one regional blood center, hospitals and blood collection facilities with the objective minimize total operational cost under centralized control. The model provides decisions on blood collection, production, and allocation. To cope with demand uncertainty coupled with the short shelf life of platelets, a five-stage scenario tree is presented and stock age information is considered. Further, the model incorporates multiple sources of supply and age-differentiated demand. The model is applied to an example from a real-world platelet supply chain. Our results show that the solution efficiency of the platelet supply chain can be obtained without following a FIFO issuing policy. They also suggest that recruiting more donors at hospitals and maintaining a minimum capacity level of 60 units at the blood center could lead to performance improvement in the platelet supply chain.

## 2.2. Introduction

The supply chain for blood and its components (i.e. red blood cells, plasma, and platelets), starting from the donor until the blood is used to meet transfusion demands of patients, is different from a traditional supply chain. Blood is an indispensable component of human life and when demand is not met, life may be lost. Maintaining adequate inventory to fulfill demand is necessary. Every day in the US, approximately 36,000 units of red blood cells, 7,000 units of platelets and 10,000 units of plasma are required in hospitals and emergency treatment facilities (American Red Cross, 2016). However, as a scarce resource, blood can only come from human donations. There are around 6.8 million donors in the US each year, only 10% of the eligible

population (American Red Cross, 2016). The daily registered blood donation is less than half of its daily demand (ABC News, 2013). Further, blood is a highly perishable product. The red cells can be stored for 42 days and the platelets must be used within 5 days (American Red Cross, 2017a). Unpredictable and unbalanced supply and demand of blood products incurs a lot of waste due to expiry. An effective blood supply chain should be able to meet the demand while at the same time reducing wastage and total operational cost.

In general, there are four main echelons in the blood supply chain: collection, production, inventory and distribution. It starts with the collection of blood from donor populations. There are three main kinds of places where blood donations can be made: bloodmobiles, blood centers, and hospitals. A bloodmobile is a large vehicle (usually a bus or a large van) equipped with necessary facilities for blood donation. It usually travels to public places such as colleges and churches to collect blood. Only whole blood units can be donated in bloodmobiles. Next, most of the blood collected from a donor will be transferred to a regional blood center, at which it will be separated into red blood cells, platelets, and plasma. At the same time, the test tubes from the same donor will be sent to a testing laboratory to perform tests for infectious diseases. The blood units will be discarded if any test result is positive. The processing and testing procedures usually take about two days. After processing and testing, blood units that are suitable for transfusion are put into inventories, either at blood centers or hospitals. The distribution process mainly includes the transport of blood products from a regional blood center to different hospitals. In addition, blood can also be transported from one blood center to another blood center or from one hospital to another hospital. The internal transfer of blood products from a hospital blood bank to the transfusion point is also possible.

Platelets are the small colorless cell fragments in blood and are mainly used to stop bleeding. According to Duan and Liao (2013), platelets are widely used in today's therapies including bone marrow transplants, organ transplants, chemotherapy, and radiation treatments. Due to the critical medical importance and highly perishable characteristic of platelets, the platelet supply chain attracts a lot of researchers in different parts of the world. However, most earlier studies didn't consider the age distribution of platelet stock when placing orders, which is contrary to the conclusion by Blake (2009) that the impact of age distribution cannot be ignored. Some recent studies (Ensafian & Yaghoubi, 2017; Gunpinar & Centeno, 2015) proposed optimization models considering stock age information and use several constraints to enforce a FIFO issuing policy. The FIFO policy can be helpful in reducing wastage if it results in older products being used first. In this study, we found that optimal performance of the platelet supply chain can be obtained without following a FIFO issuing policy.

This study will explore opportunities to optimize the multi-echelon platelet supply chain by minimizing the total operational cost under centralized control. In a centralized control system, centralized production decisions are made for all participants of the supply chain to directly minimize the system-wide operational cost instead of minimizing individual operational cost for each participant independently. In this study, we developed a novel multi-stage stochastic optimization model for integrated collection, production, inventory, and distribution of platelets considering stock age information. Apheresis and whole blood collection are both incorporated into the mathematical model. Three types of patients have been categorized for platelet demand in different age ranges. The model is applied to an example from a real-world platelet supply chain. Impacts of a FIFO policy, available donors at hospitals, and capacity level

at the blood center are investigated to examine potential performance improvement in the supply chain.

### 2.3. Literature review

The blood supply chain has been broadly studied by researchers from different parts of the world. Some of the earliest studies date back to the 1970s and 1980s (Cohen, 1979; Jennings, 1973; Kendall & Lee, 1980; Prastacos, 1984). Prastacos (1984) provided a comprehensive review of the main contributions from operations research to blood inventory management and identified several important issues for future research. For more recent studies, Beliën and Forcé (2012) presented a review for supply chain management and inventory models of different blood products which covered papers published up to 2010, and Osorio et al. (2015) provided a literature review on the blood product supply chain which focused on quantitative models and presented the main features of each model based on the relevant supply chain echelon. Osorio et al. (2015) divided these models into five categories: four categories represent the four echelons (stages) in the supply chain: collection, production, inventory and distribution, and one category represents integrated models that involve at least two echelons. Most studies on the blood supply chain have focused on a single echelon and ignored the relationships between different stages. Models for individual echelons include collection (Godin et al., 2007; Salehi et al., 2017), production (Ghandforoush & Sen, 2010; Haijema et al., 2009), inventory (Blake et al., 2010; Hosseinifard & Abbasi, 2018) and distribution (Hemmelmayr et al., 2010; Civelek et al., 2015). At the same time, there are still several studies that model the blood supply chain as a two or multi-echelon system (Arvan et al., 2015; Fahimnia et al., 2015; Fereiduni et al., 2016; Jabbarzadeh et al., 2014; Kaveh & Ghobadi, 2016; Kohneh et al., 2016; Osorio et al., 2016).

Platelets have a very short shelf life compared to other blood products (i.e. red blood cells), making balancing shortage and wastage even harder and even more important. According to Blake (2009), age distribution of inventory plays an very important role in the supply chain management of platelets. Earlier works ignored the age information when placing an order, while more recent works consider an age-based inventory model for blood products (Abdulwahab & Wahab, 2014; Duan & Liao, 2013, 2014; Ensafian & Yaghoubi, 2017; Ensafian et al., 2017; Gunpinar & Centeno, 2015; Wang & Ma, 2015). To our knowledge, Duan and Liao (2013) were the first to develop a quantitative model of platelet supply chain inventory that considers age information. They proposed an age-based replenishment policy called the old inventory ratio (OIR) and compared it with two existing order-up-to policies and proved the superiority of the OIR policy. To minimize total cost including shortage and wastage costs at hospitals, Gunpinar and Centeno (2015) proposed three integer programming models considering age-differentiated demand rates. Their supply chain under investigation considered two types of patients, type 1 patients can only use platelets younger than three days old and type 2 patients can use platelets of any age. Ensafian and Yaghoubi (2017) presented an integrated platelet supply chain including procurement, production and distribution of platelets. Three different patient types and age information of platelets were considered. This paper introduced three deterministic models in which FIFO, LIFO and Bi-objective issuing policies were investigated using two stochastic models to deal with demand uncertainty. Also, Ensafian et al. (2017) developed a two-stage stochastic programming model that incorporated the age of platelets and ABO-Rh priority matching rules. A policy with age information was shown to be superior to policies without age considerations (Tekin et al., 2001), so age information of blood products will be considered in this research.

Demand uncertainty considerably complicates management of blood products, thus most research in this area assumed that demand is deterministic or its uncertainty can modelled as a Poisson or Normal distribution. Samani and Hosseini-Motlagh (2018) summarized four common approaches to deal with uncertainty: fuzzy, robust, robust-fuzzy and stochastic programming. Among them, stochastic programming models are most commonly used (Abdulwahab & Wahab, 2014; Dillon et al., 2017; Ensafian et al., 2017; Rajendran & Ravindran, 2017; Zahiri et al., 2018). To minimize the platelet shortages and wastage while maximizing total rewards, Abdulwahab and Wahab (2014) proposed an approximate dynamic programming model for a blood platelet bank considering ABO-Rh blood types, platelet age, stochastic demand, stochastic supply, and deterministic lead time. In order to find optimal periodic review policies for red blood cells, Dillon et al. (2017) developed a two-stage stochastic program considering perishability and demand uncertainty. Zahiri et al. (2018) presented a multi-stage stochastic program for an integrated blood supply chain to simultaneously minimize total cost and maximize residual shelf life of delivered blood products.

In this study, we develop a multi-stage stochastic program for an integrated platelet supply chain which takes into account demand uncertainty, age information, two types of supply sources and three types of patients. The objective is to provide tactical and operational decisions on blood collection, production, and allocation. Our study contributes to the literature in four ways. First, we present a multi-stage stochastic program that incorporates all echelons in the platelet supply chain. A multi-stage stochastic program performs better than a two-stage program in reflecting and representing demand uncertainties. Second, we use a real-world case to validate the developed model, which is rare in the literature of blood supply chain management (see Beliën & Forcé, 2012). Third, we observed that it is not necessary for researchers to enforce

constraints regarding following a FIFO issuing policy to achieve an optimal performance when optimizing the platelet supply chain. Finally, we found that recruiting more donors at hospitals and maintaining a minimum capacity level of 60 units at the blood center could lead to improvement in the platelet supply chain performance.

## 2.4. Problem description and model formulation

The scope of this study focuses on modeling a supply chain of platelets in one regional blood center with several hospitals and blood collection facilities. In order to be cost effective in the process starting with collecting blood from donors and ending with transfusion of platelets before their shelf life has expired, the related organizations have to investigate how much blood or single blood components should be collected from donors, how much platelets should be produced in the blood center, and how much platelets should be transferred to hospitals in each period. Therefore, we consider an integrated supply chain including all stages of collection, production, and distribution of platelets and the objective is to minimize the total operational cost.

### 2.4.1. Problem description

Consider the platelet supply chain as depicted in Figure 3. Supply of platelets can be classified into two types by different sources, which are whole blood derived and apheresis derived. Apheresis is the process of collecting a specific component of the blood, such as red blood cells, plasma, or platelets, and returning the remaining components back to the donor. The number of platelets collected from one apheresis donation would normally equal up to four to six times that of whole blood donations (American Red Cross, 2017b). In general, there are two kinds of blood collection facilities: permanent and temporary. Apheresis derived platelets can

only be collected from permanent facilities such as hospitals and blood centers, while donors can visit both permanent and temporary facilities to donate whole blood.

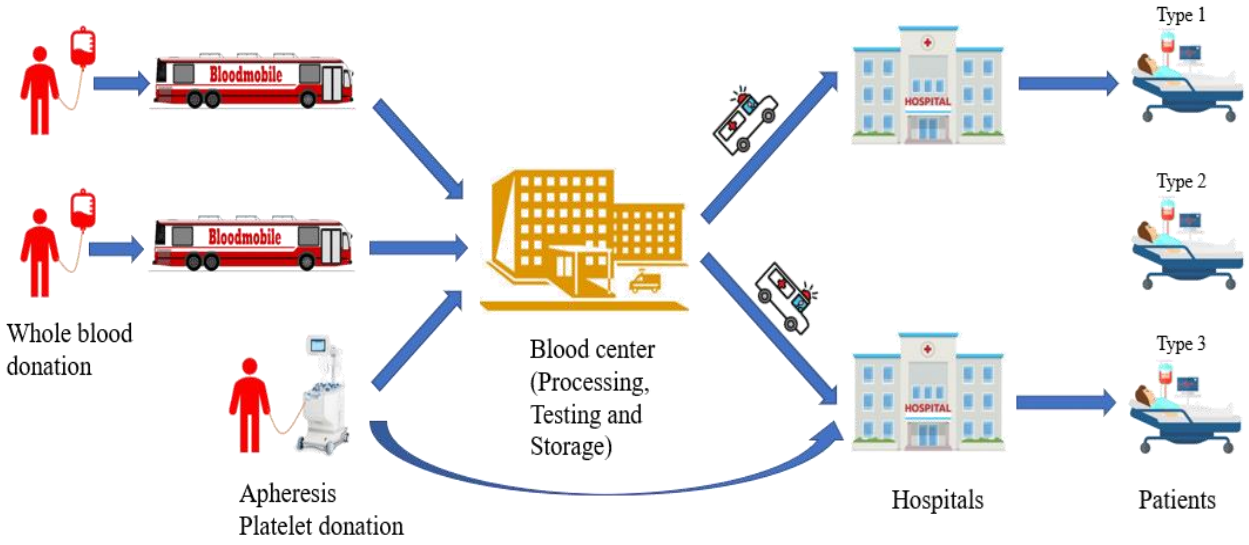


**Figure 3. Platelet supply chain network**

Blood units collected from registered donors at different blood collection facilities are sent to the regional blood center for testing and production of blood components. Usually, it will take two days for testing and processing after collection. But for apheresis derived platelets, only one day is needed for bacterial testing. The transfusion demand and production schedule of platelets differ by day of the week. At the start of each work day the blood center distributes certain units of platelets to the hospitals it serves based on relevant orders. During the day, on one hand, blood is collected using bloodmobiles at blood collection facilities and platelets are produced at the blood center, on the other hand, hospitals issue available units of platelets to satisfy patient demand. At the end of the working day, all outdated platelets are removed from inventory and the inventory statuses for the blood center and hospitals are updated. New orders for each hospital are decided and a new production plan for the blood center is identified without knowing demand. Unlike the blood center, the units received by hospitals may not be of the same

age upon arrival and different hospitals may have different age distributions. Lead times for orders from the blood center are assumed to be zero.

Platelet demand can be categorized by three patient types. See Table 2 (Ensafian & Yaghoubi, 2017). The demand for Type 1 patients who need bone marrow or organ transplants can only be satisfied with fresh platelets (1 day old). The demand for Type 2 patients which are oncology and hematology cases should be satisfied with young platelets (no more than 3 days old). Type 3 patients can use platelets of all ages up to the maximum shelf life.

**Table 2. Age of platelets and related usage**

| Demand Type | Age | Case of usage |
|---|---|---|
| Fresh | 1 day old | Bone marrow transplants |
| Young | 2-3 days old | Oncology and hematology |
| Old | 4-5 days old | Traumatology and general surgery |

### 2.4.2. Multi-stage stochastic programming approach

The demand for blood platelets in hospitals is not fixed and may fluctuate over time, so demand uncertainty must be considered. Stochastic programming is specifically used to deal with modeling problems that involve uncertainty (see Birge & Louveaux, 2011). It can be categorized as two-stage and multi-stage programming in terms of stages.

In a two-stage framework, decision variables are categorized into two groups: first stage and second stage variables. The first-stage decisions, also called “here-and-now” decisions, are independent of scenarios and are made prior to the realization of uncertainty. The second-stage decisions, referred to as “wait-and-see” decisions, represent a collection of scenario-dependent recourse actions that are determined to account for changes after the uncertainty is revealed. The two stage stochastic programming approach is often used in a single-period environment (Birge

& Louveaux, 2011). In contrast, a multi-stage stochastic program is adopted to deal with a dynamic environment where information is slowly revealed over time.

Multi-stage stochastic programs involve a sequence of decisions that respond to realized outcomes that are unknown a priori. In our study, the first-stage decisions mainly include the supply of whole blood and apheresis derived platelets in the blood center. The second stage decisions are those referring to the operation of the blood center and hospitals in the first day, specifically, the production, distribution, inventory, shortage, and wastage. The third stage decisions refer to the operation of both the blood center and hospitals on the second day when information from the first day is known. This decision-making process repeats till the last day of the planning horizon.

### 2.4.3. Model formulation

In this section, a scenario-based multi-stage stochastic program is formulated to deal with the integrated platelet supply chain.

#### *2.4.3.1. Notation*

The indices, parameters and decision variables used in the mathematical model are as follows.

**Table 3. Notation used in the platelet supply chain model**

| **Indices** | **Description** |
|---|---|
| $n$ | Age of platelets, $n \in N$ |
| $k$ | Demand type for platelets, $k \in K = \{1,3,5\}$ |
| $i, m$ | Hospitals, $i, m \in I$ |
| $j$ | Blood collection facilities, $j \in J$ |
| $t$ | Time periods, $t \in T$ |
| $\varepsilon$ | Scenarios, $\varepsilon \in$ E |
| | |
| **Parameters** | |
| $N$ | Maximum shelf life of platelets |
| $\beta$ | The amount of platelet units collected from a donor by apheresis |
| $\theta$ | Proportion of whole blood collected used for producing platelets |

**Table 3. Notation used in the platelet supply chain model (continued)**

| **Parameters** | **Description** |
|---|---|
| $\gamma$ | Percentage of whole blood units which are not appropriate for platelet production |
| $H_i$ | Transportation cost per unit from the blood center to hospital $i$ |
| $G_j$ | Transportation cost per unit from collection facility $j$ to the blood center |
| $F$ | Set up cost of producing platelets from whole blood at the blood center |
| $V$ | Variable cost of producing one unit of platelet from whole blood at the blood center |
| $p$ | Production cost of one unit of apheresis platelet at the blood center and hospitals |
| $h$ | Holding cost per unit per day |
| $u$ | Shortage cost per unit |
| $v$ | Outdating cost per unit |
| $d_{itk\varepsilon}$ | Patient demand of type $k$ for platelets at hospital $i$ on day $t$ under scenario $\varepsilon$ |
| $D_k$ | Set of platelet ages associated with demand type $k$ |
| $W_{jt}$ | Number of available whole blood donors at collection facility $j$ on day $t$ |
| $X_{it}$ | Number of available platelet donors at hospital $i$ on day $t$ |
| $X_{0t}$ | Number of available platelet donors at the blood center on day $t$ |
| $C_i$ | Capacity at hospital $i$ |
| $C_0$ | Platelet production capacity for the blood center |
| $P_\varepsilon$ | Probability that scenario $\varepsilon$ will happen |
| | |
| **Variables** | |
| $B_{jt}$ | Quantity of whole blood collected from collection facility $j$ on day $t$ |
| $Q_t$ | Quantity of platelets produced from whole blood at the blood center on day $t$ |
| $A_{it}$ | Quantity of platelet apheresis at hospital $i$ on day $t$ |
| $A_{0t}$ | Quantity of platelet apheresis at the blood center on day $t$ |
| $I_{itn\varepsilon}$ | The quantity of platelets aged $n$ in the inventory of hospital $i$ at the beginning of day $t$ under scenario $\varepsilon$ |
| $I_{0tn\varepsilon}$ | The quantity of platelets aged $n$ in the inventory of the blood center at the beginning of day $t$ under scenario $\varepsilon$ |
| $O_{it\varepsilon}$ | Outdated quantity at hospital $i$ on day $t$ under scenario $\varepsilon$ |
| $O_{0t\varepsilon}$ | Outdated quantity at the blood center on day $t$ under scenario $\varepsilon$ |
| $S_{itk\varepsilon}$ | Shortage quantity of platelets for demand type $k$ at hospital $i$ on day $t$ under scenario $\varepsilon$ |
| $U_{itn\varepsilon}$ | The amount of platelet units aged $n$ in the inventory of hospital $i$ used to satisfy demand on day $t$ under scenario $\varepsilon$ |
| $R_{itn\varepsilon}$ | The amount of platelet units aged $n$ received by hospital $i$ on day $t$ under scenario $\varepsilon$ |
| $Z_t$ | 1 if platelets are produced at the blood center on day $t$, 0 otherwise |

### *2.4.3.2. Mathematical model*

In this section, we propose an integrated platelet supply chain model which includes all stages of collection, production, and distribution. Whole blood or apheresis platelets are collected from registered donors in blood collection facilities when an order is issued from the regional blood center, then the blood units are delivered from the blood center to different hospitals based on the daily demand, and finally hospital blood banks categorize the received platelet units by age group and use them for different medical treatments. Therefore, the following decisions need to be optimized: the amount of blood units to be collected from donors, the amount of platelet units to be produced, and the assignment of platelet units to hospitals.

The mathematical formulation for the problem is given as follows:

$$Min\ \sum_{t=1}^{T} F \cdot Z_t + \sum_{t=1}^{T} V \cdot Q_t + \sum_{t=1}^{T} p \cdot A_{0t} + \sum_{t=1}^{T}\sum_{i=1}^{N} p \cdot A_{it} + \sum_{t=1}^{T}\sum_{j=1}^{J} G_j \cdot B_{jt} + \sum_{\varepsilon}\sum_{t=1}^{T}\sum_{i=1}^{I}\sum_{n=1}^{N} P_\varepsilon \cdot H_i \cdot R_{itn\varepsilon} + \sum_{\varepsilon}\sum_{t=1}^{T}\sum_{i=1}^{I}\sum_{n=1}^{N} P_\varepsilon \cdot h \cdot I_{itn\varepsilon} + \sum_{\varepsilon}\sum_{t=1}^{T}\sum_{n=1}^{N} P_\varepsilon \cdot h \cdot I_{0tn\varepsilon} + \sum_{\varepsilon}\sum_{k=1}^{K}\sum_{t=1}^{T}\sum_{i=1}^{I} P_\varepsilon \cdot u \cdot S_{itk\varepsilon} + \sum_{\varepsilon}\sum_{t=1}^{T}\sum_{i=1}^{I} P_\varepsilon \cdot v \cdot O_{it\varepsilon} + \sum_{\varepsilon}\sum_{t=1}^{T} P_\varepsilon \cdot v \cdot O_{0t\varepsilon} \quad (2.1)$$

s.t.

$$Q_t \le C_0 \cdot Z_t \qquad \forall t \quad (2.2)$$

$$\sum_{n=1}^{N-1} I_{0tn\varepsilon} \le C_0 \qquad \forall t, \varepsilon \quad (2.3)$$

$$\sum_{n=1}^{N-1} I_{itn\varepsilon} \le C_i \qquad \forall i, t, \varepsilon \quad (2.4)$$

$$B_{jt} \le W_{jt} \qquad \forall j, t \quad (2.5)$$

$$A_{it} \le X_{it} \qquad \forall i, t \quad (2.6)$$

$$A_{0t} \le X_{0t} \qquad \forall t \quad (2.7)$$

$$\sum_{j=1}^{J} B_{jt} \cdot \theta \cdot (1-\gamma) \ge Q_{t+2} \qquad t = 0, \dots, T-2 \quad (2.8)$$

$$I_{0(t+1)n\varepsilon} = I_{0t(n-1)\varepsilon} - \sum_{i=1}^{I} R_{it(n-1)\varepsilon} \qquad t = 1, \dots, T-1, n = 3, \dots, N, \varepsilon \quad (2.9)$$

$$I_{0(t+1)2\varepsilon} = Q_{t+1} + I_{0t1\varepsilon} - \sum_{i=1}^{I} R_{it1\varepsilon} \qquad t = 1, \dots, T-1, \varepsilon \tag{2.10}$$

$$I_{0t1\varepsilon} \geq \sum_{i=1}^{I} R_{it1\varepsilon} \qquad t = 1, \dots, T-1, \varepsilon \tag{2.11}$$

$$I_{0(t+1)1\varepsilon} = \beta \cdot A_{0t} \qquad t = 0, \dots, T-1 \tag{2.12}$$

$$I_{i(t+1)1\varepsilon} = \beta \cdot A_{it} \qquad \forall i, t = 0, \dots, T-1, \varepsilon \tag{2.13}$$

$$I_{i(t+1)n\varepsilon} = R_{it(n-1)\varepsilon} + I_{it(n-1)\varepsilon} - U_{it(n-1)\varepsilon} \qquad \forall i, t = 1, \dots, T-1, n = 2, \dots, N, \varepsilon \tag{2.14}$$

$$U_{it1\varepsilon} + S_{it1\varepsilon} \geq d_{it1\varepsilon} \qquad \forall i, t, \varepsilon \tag{2.15}$$

$$\sum_{n=1}^{3} U_{itn\varepsilon} + S_{it1\varepsilon} + S_{it3\varepsilon} \geq d_{it1\varepsilon} + d_{it3\varepsilon} \qquad \forall i, t, \varepsilon \tag{2.16}$$

$$\sum_{n=1}^{5} U_{itn\varepsilon} + S_{it1\varepsilon} + S_{it3\varepsilon} + S_{it5\varepsilon} \geq d_{it1\varepsilon} + d_{it3\varepsilon} + d_{it5\varepsilon} \qquad \forall i, t, \varepsilon \tag{2.17}$$

$$I_{itn\varepsilon} = O_{it\varepsilon} \qquad \forall i, t, n = N, \varepsilon \tag{2.18}$$

$$I_{0tn\varepsilon} = O_{0t\varepsilon} \qquad \forall i, t, n = N, \varepsilon \tag{2.19}$$

$$I_{01n\varepsilon} = 0 \qquad \forall n, \varepsilon \tag{2.20}$$

$$I_{i1n\varepsilon} = 0 \qquad \forall i, n, \varepsilon \tag{2.21}$$

$$Q_t = 0 \qquad t = 1 \tag{2.22}$$

$$B_{jt}, Q_t, A_{it}, A_{0t}, O_{it\varepsilon}, O_{0t\varepsilon}, I_{itn\varepsilon}, I_{0tn\varepsilon}, S_{itk\varepsilon}, R_{itn\varepsilon}, U_{itn\varepsilon} \geq 0, \tag{2.23}$$

$$Z_t \in \{0,1\} \tag{2.24}$$

The objective function (2.1) seeks to minimize the total operational cost. This cost includes set up and variable production costs (if platelets are produced from whole blood at the blood center), production costs of apheresis platelets at the blood center and hospitals, transportation cost from collection facilities to the blood center and from the blood center to hospitals, inventory holding cost at the blood center and hospitals, shortage and outdate costs.

Constraints (2.2) and (2.3) are the capacity constraints of the blood center. Constraint (2.4) states the capacity constraints of each hospital. Constraints (2.5) - (2.7) put upper limits on

the number of whole blood donors at collection facilities and apheresis platelet donors at hospitals and the blood center, respectively. Constraint (2.8) is a balance constraint for whole blood collected and platelets produced considering two days used for processing and testing. Not all of the whole blood collected is rich enough to produce platelets; thus, $\gamma$ represents the percentage of whole blood donations not used for platelet production. Constraints (2.9) – (2.12) are balance constraints for platelet inventories at the blood center at the beginning of each day for each age group. Constraint (2.9) shows that platelet inventory that is more than two days old equals the inventory remaining from the previous period minus the quantity of units shipped to hospitals in the previous day. Constraint (2.10) updates the two-day-old inventory. Because two days are required for processing and testing, whole blood derived platelets in each day are assigned to the three-day-old inventory. Constraint (2.11) enforces the upper limit on the number of platelets shipped from the blood center to hospitals. Constraint (2.12) shows that one-day-old inventory equals the quantity of platelets produced by apheresis in the previous day as one day is used for testing apheresis derived platelets.

Constraints (2.13) and (2.14) are balance constraints for platelet inventories at hospitals at the beginning of each day based on age group. Constraint (2.13) shows that one-day-old inventory equals the quantity of platelets produced by apheresis at hospitals in the previous day. Constraint (2.14) shows that platelet inventory that is more than one day old equals the inventory remaining from the previous period and the quantity of platelets received from the blood center minus the quantity of units used to satisfy demand in the same day. Constraints (2.15) – (2.17) associate ages of platelets with different patient demand types and capture the shortage quantity for each demand type at hospitals on each day. Three patient types are considered, bone marrow or organ transplant patients can only be satisfied with fresh platelets (1 day old), oncology and

hematology patients require young platelets (2 or 3 days old) and patients who do not require frequent transfusions or a large transfusion can use platelets of all ages up to the maximum shelf life. Constraints (2.18) and (2.19) identify the outdated quantity for hospitals and the blood center, respectively. Constraints (2.20) and (2.21) state that there is no inventory at the beginning of the planning horizon at the blood center and hospitals. Constraint (2.22) states that there is no platelet inventory derived from whole blood in the first two days as two days are needed for testing and processing. Constraint (2.23) shows $B_{jt}, Q_t, A_{it}, A_{0t}, O_{it\varepsilon}, O_{0t}, I_{itn\varepsilon}, I_{0tn}, S_{itk\varepsilon}, R_{itn\varepsilon}$ and $U_{itn\varepsilon}$ are non-negative, and constraint (2.24) states that $Z_t$ is a binary variable.

## 2.5. Computational study

### 2.5.1. Case description

In this section, an example from a real-world platelet supply chain is presented to demonstrate possible applications of the proposed model. The supply chain consists of 3 collection facilities and one regional blood center which provides platelets for 5 registered hospitals in the Fargo-Moorhead area. Registered hospitals are those hospital facilities that meet the registration requirements of the American Hospital Association. According to data collected for the blood collection facilities of the local blood center in a four-month period, we found that more than 50 different geographical locations were available while only around 3 of them would be visited per week. Therefore, we randomly picked one week when three collection facilities were visited in our case study. The geographical location of collection facilities, the blood center and hospitals are shown in Figure 4.

The planning horizon time was considered as six days since the lifetime of platelets is five days and any unused platelets will be removed from inventory at the beginning of the sixth day. According to the American Red Cross, the number of platelets collected by apheresis equals

up to four to six times that of whole blood donations, we considered that one unit of platelets could be drawn from one unit of whole blood while six units of platelets could be obtained from a donor using apheresis. Not all the whole blood units collected are suitable for producing platelets, a value of 2% was used for $\gamma$ based on Ensafian and Yaghoubi (2017).

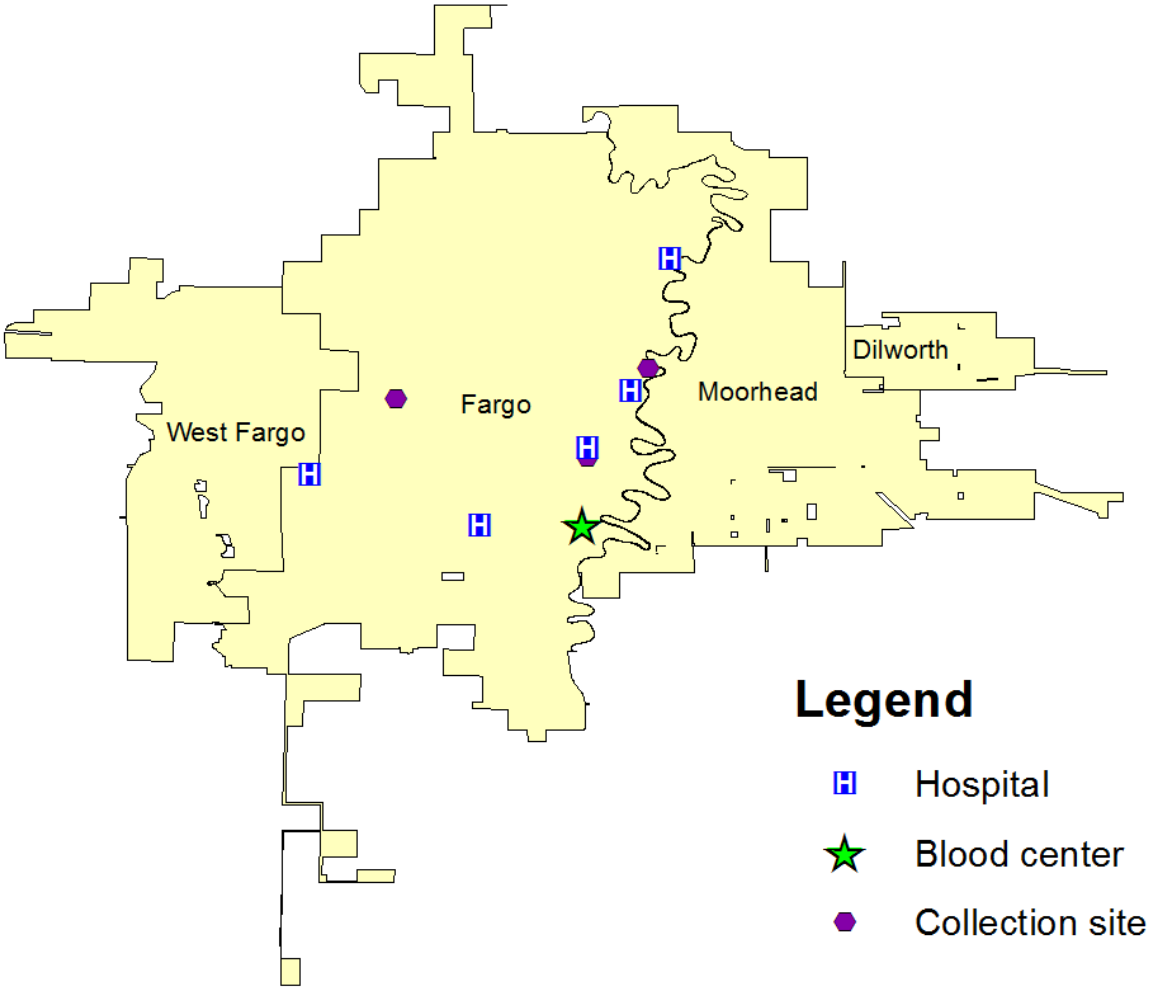


**Figure 4. The proposed platelet supply chain in the Fargo-Moorhead area**

#### *2.5.1.1. Data*

Table 4 summarizes the values of cost parameters that were used in the models. Apheresis production, holding, shortage, and outdating costs were obtained from Gunpinar and Centeno (2015). Fixed and variable production cost of whole blood derived platelets was taken

from Ensafian and Yaghoubi (2017). Table 5 presented the value of transportation cost from the blood center to hospitals and from collection facilities to the blood center. The cost was estimated to be proportional to the geographical distance between two locations. The unit shipping cost for blood products with a distance of 5.2 miles was assumed to be $1 per unit in accordance with the transfer cost presented by Ensafian and Yaghoubi (2017).

**Table 4. Cost parameters**

| Parameters | Value | Units | Reference |
|---|---|---|---|
| Set up cost | 1 | $/unit | Ensafian & Yaghoubi (2017) |
| Variable production cost | 150 | $/unit | Ensafian & Yaghoubi (2017) |
| Apheresis production cost | 538 | $/unit | Gunpinar & Centeno (2015) |
| Holding cost | 1.25 | $/unit | Gunpinar & Centeno (2015) |
| Shortage cost | 1500 | $/unit | Gunpinar & Centeno (2015) |
| Outdating cost | 150 | $/unit | Gunpinar & Centeno (2015) |

**Table 5. Transportation cost**

| Location | Distance to the blood center (mile) | Value ($/unit) |
|---|---|---|
| Collection facility 1 | 5.2 | 1 |
| Collection facility 2 | 4.4 | 0.85 |
| Collection facility 3 | 1.7 | 0.33 |
| Hospital 1 | 10.6 | 2.04 |
| Hospital 2 | 5 | 0.96 |
| Hospital 3 | 3.3 | 0.63 |
| Hospital 4 | 1.6 | 0.31 |
| Hospital 5 | 1.6 | 0.31 |

The number of available donors in each period is presented in Table 6. The number was estimated using real data for available appointments in each collection facility, the blood center and hospitals under a 4-month period.

**Table 6. Number of available donors**

| Type of donors | Value (unit) |
|---|---|
| Whole blood donors at collection facilities | Uniform ~ [15,25] |
| Platelet donors at the blood center | Uniform ~ [10,15] |
| Platelet donors at hospitals | Uniform ~ [0,5] |

Table 7 presents the mean value for daily demand at each hospital which was based on previous studies on platelet supply chain management (Ensafian & Yaghoubi, 2017; Haijema et al., 2007). The demand in each period was assumed to follow a Poisson distribution and to be independent of other periods. The five hospitals considered were classified based on the number of hospital beds and a demand coefficient was assigned to estimate average daily demand of hospitals in each category. According to Ensafian and Yaghoubi (2017), the demand coefficient for a hospital with number of beds in the category of 100-150 is 1. Haijema et al. (2007) stated that approximately 70% of platelet demand was for young and fresh platelets and 30% was for old platelets. We assumed that consumption proportion for young, fresh and old demand types was 20%, 50% and 30%, respectively

**Table 7. Mean daily demand at each hospital in each period**

| Days | Hospital 1 | Hospital 2 | Hospital 3 | Hospital 4 | Hospital 5 |
|---|---|---|---|---|---|
| 1 | 18 | 42 | 24 | 12 | 24 |
| 2 | 12 | 28 | 16 | 8 | 16 |
| 3 | 24 | 56 | 32 | 16 | 32 |
| 4 | 12 | 28 | 16 | 8 | 16 |
| 5 | 18 | 42 | 24 | 12 | 24 |

#### *2.5.1.2. Scenario generation*

A scenario tree is used to represent the abstract structure of scenarios which include all possible combinations of outcomes for discrete random events in a multi-stage stochastic

program. Figure 5 shows a schematic view of the 5-stage scenario tree used in this study with 63 nodes, which denotes 32 scenarios in a dynamic planning environment. Each node denotes a different level of demand and each arc corresponds to each stage.

In the beginning of each stage, two demand scenarios for each hospital are obtained using random numbers generated from MATLAB that follow a Poisson distribution with mean value as shown in Table 7. The two demand scenarios generated for each day are combined with other days to make a total of 32 scenarios in the six-day planning horizon. For the multi-stage formulation, non-anticipativity constraints must be enforced. Non-anticipativity is defined as the value of a decision variable only depending on historical information and being independent of future observations. In this study, the decision variable that denotes the quantity of platelets received by hospitals ($R_{itn\varepsilon}$) needs to satisfy the non-anticipativity constraints which are shown in Figure 5. For example, "R11=R12=…=R115=R116" means that the quantity of platelets in each age group received by each hospital on the first day are the same for the first 16 scenarios.

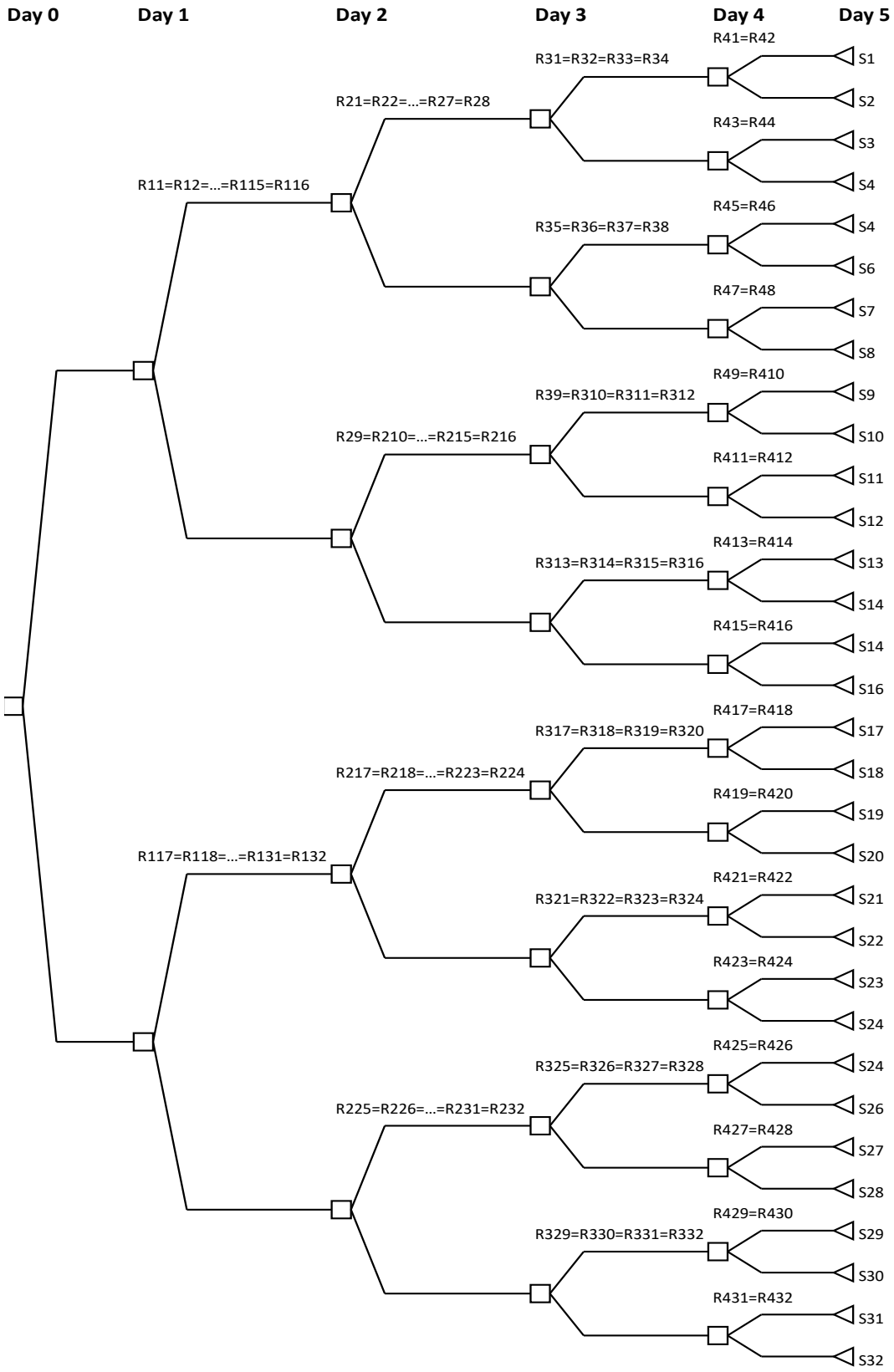


**Figure 5. A schematic view of the scenario tree for demand**

### 2.5.2. Numerical results

The multi-stage stochastic program was solved using IBM ILOG CPLEX 12.8 optimizer on a Dell OPTIPLEX 9020 computer running with 3.40 GHz CPU and 16GB of RAM. The proposed model had 24,722 constraints and 29,869 variables with 32 scenarios.

Table 8 summarized computational results of daily cost in the planning period. The total operational cost for the proposed model is $76,472. Production cost was the largest and shortage cost was the second largest. The total quantity of platelet shortage is 15 units and most of the shortages took place in the first day. This is to be expected as there was no initial platelet inventory at the beginning of the planning horizon. No outdates occurred within the time period. Figure 6 shows the result of blood collection at the blood center and hospitals using apheresis on different days. Though platelets can be collected using two methods which include whole blood derived and apheresis derived approaches, our numerical result indicates that all platelets were produced using apheresis. Platelets collected by apheresis are more cost effective than those by whole blood. Though production cost for platelet apheresis is higher than whole blood separation, the unit production cost is actually cheaper as six units of platelets could be obtained from a donor using apheresis. For each day, if the blood center collects more units of platelets, hospitals will collect less, and vice versa. Figure 7 shows the result of demand realization under different scenarios. The number of platelets used to satisfy demand fluctuates for different scenarios on different days. This result is consistent with the generated daily demand in hospitals under relevant scenarios. Figure 8 shows the result of daily inventory at different hospitals. Most hospitals have higher inventory on day 2 and day 4. This is because for each hospital mean daily demand on these two days is lower than on other days. As less platelets are used to satisfy demand, more blood units will be left and put into inventory.

**Table 8. Results of daily cost**

| Days | Total cost | Production cost | Transportation cost | Inventory holding cost | Shortage cost | Outdate cost |
|---|---|---|---|---|---|---|
| 1 | 33,451 | 10,760 | 41 | 150 | 22,500 | 0 |
| 2 | 10,925 | 10,760 | 11 | 154 | 0 | 0 |
| 3 | 12,133 | 11,836 | 72 | 225 | 0 | 0 |
| 4 | 9,301 | 9,146 | 8 | 147 | 0 | 0 |
| 5 | 10,661 | 10,222 | 25 | 179 | 234 | 0 |
| Total | 76,472 | 52,724 | 158 | 856 | 22,734 | 0 |

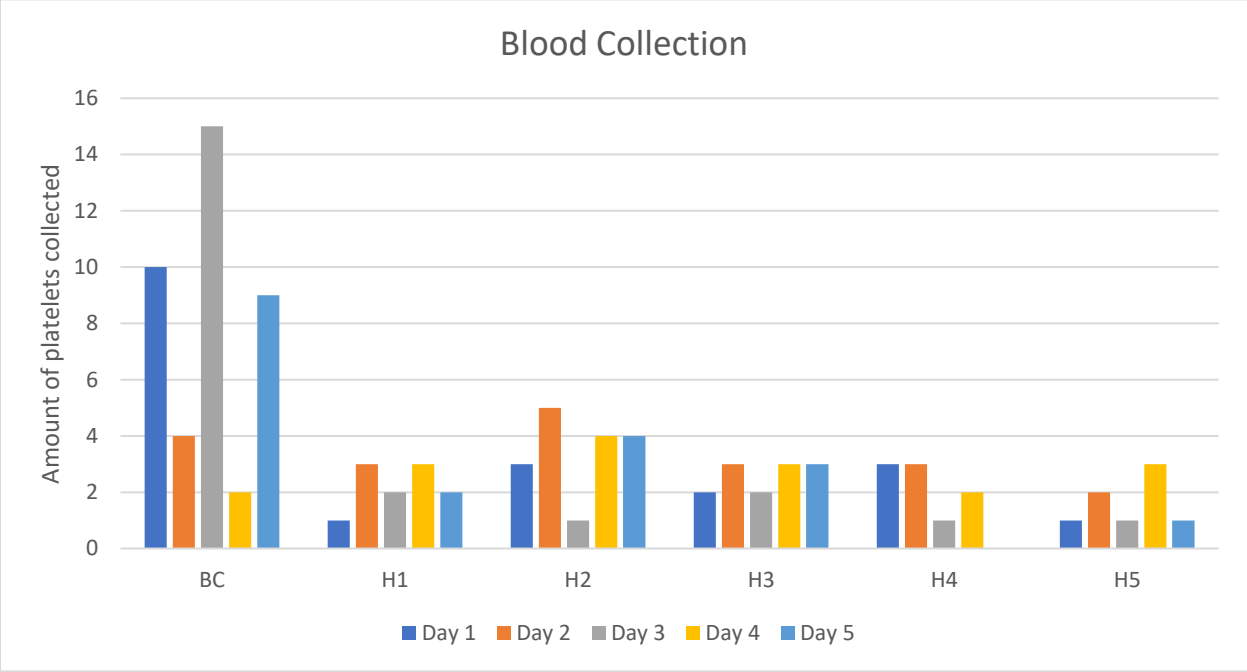


**Figure 6. Result of blood collection at the blood center and hospitals**

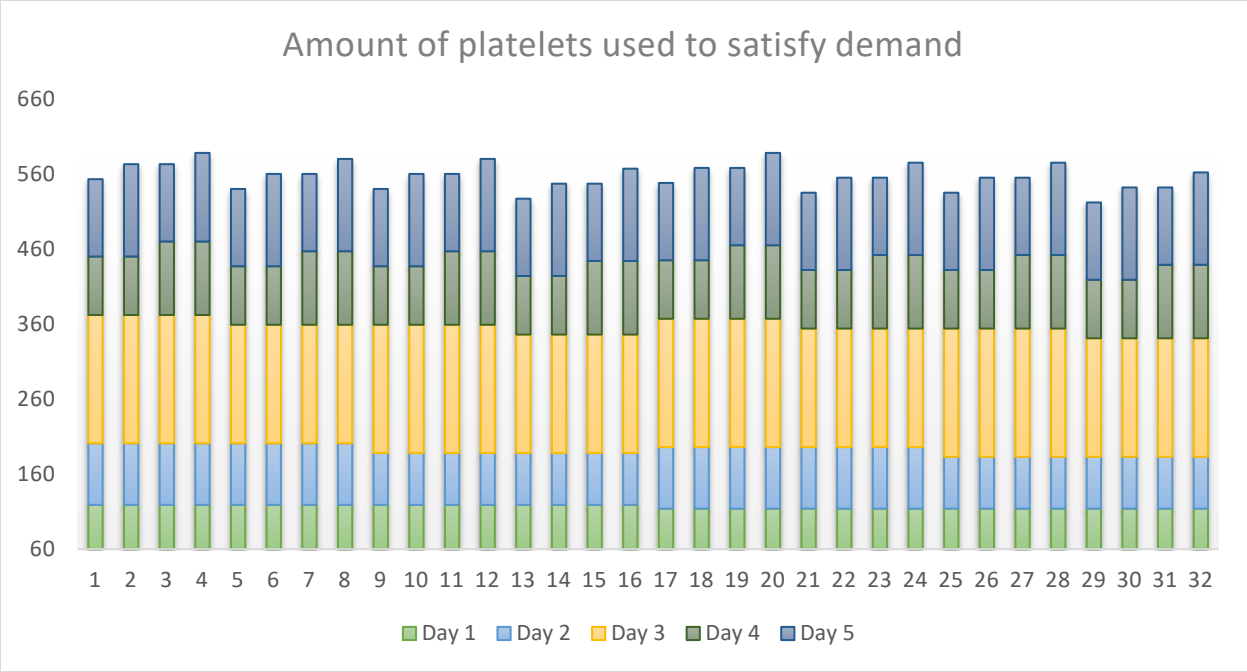


**Figure 7. Result of demand realization under different scenarios**

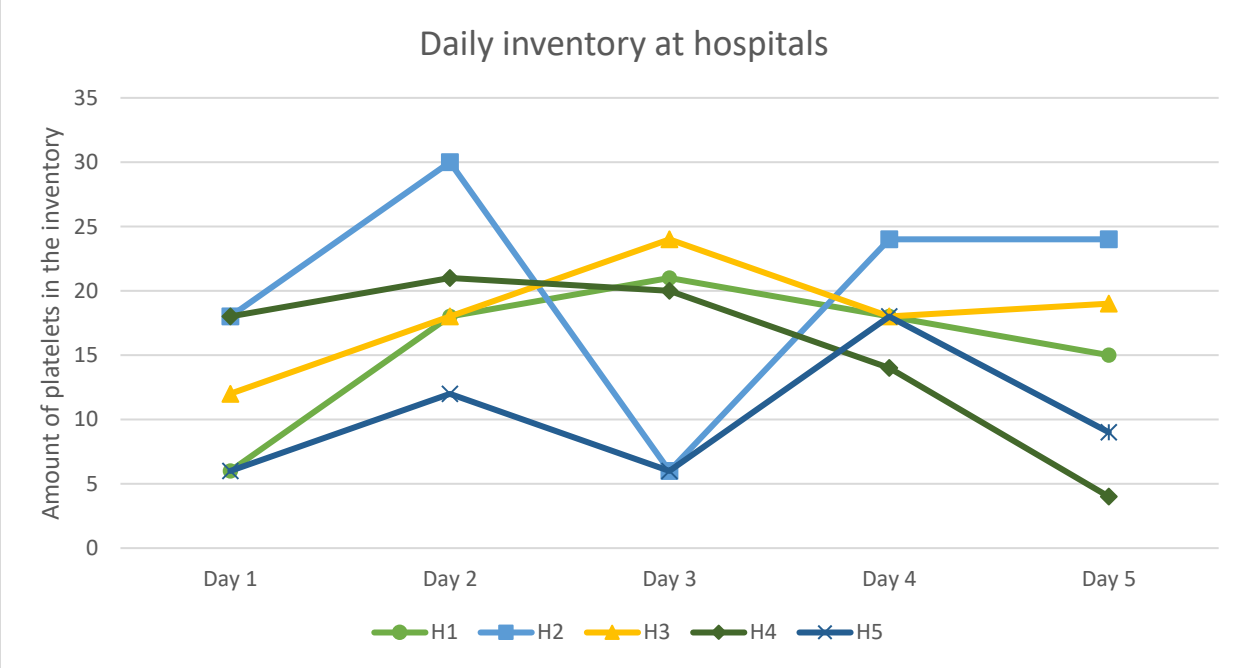


**Figure 8. Result of daily inventory at hospitals**

### 2.5.3. Sensitivity analysis

#### *2.5.3.1. Impact of a FIFO policy*

A FIFO issuing policy is encouraged for perishable supply chains. FIFO can often help with reducing wastage and total cost since products near expiry may be used first. Therefore, two recent studies (Ensafian & Yaghoubi, 2017; Gunpinar & Centeno, 2015) used several constraints to enforce a FIFO issuing policy when developing optimization models for the blood supply chain. In this study, we did not enforce a FIFO issuing policy so that we could assess if the optimal policy was naturally consistent with a FIFO policy. However, our numerical results indicate that a FIFO policy was not followed at either the blood center or the hospitals.

In order to evaluate the impact of a FIFO policy on the supply chain, we incorporated two decision variables and developed a stochastic mixed integer program under a FIFO policy (see Table 9).

**Table 9. Additional parameters and decision variables under FIFO policy**

| **Parameters** | **Description** |
|---|---|
| $M$ | A big number |
| **Decision variables** | |
| $Y_{0tn\varepsilon}$ | 1 if platelets aged $n$ in the inventory of the blood center are used to satisfy demand on day $t$ under scenario $\varepsilon$, 0 otherwise |
| $Y_{itn\varepsilon}$ | 1 if platelets aged $n$ in the inventory of hospital $i$ are used to satisfy demand on day $t$ under scenario $\varepsilon$, 0 otherwise |

The model uses the same objective function (2.1) and constraints (2.2) – (2.24) and the following constraints (2.25) – (2.31) for FIFO issuance decisions in the platelet supply chain.

$$\sum_{i=1}^{I} R_{itn\varepsilon} \leq M \cdot Y_{0tn\varepsilon} \qquad \forall i, t, n, \varepsilon \qquad (2.25)$$

$$M \cdot \left(1 - Y_{0t(n-1)\varepsilon}\right) \geq I_{0tn\varepsilon} - \sum_{i=1}^{I} R_{itn\varepsilon} \qquad \forall i, t, n = 3{,}5, \varepsilon \qquad (2.26)$$

$$Y_{0tn\varepsilon} \geq Y_{0t(n-1)\varepsilon} \qquad \forall i, t, n = 3{,}5, \varepsilon \qquad (2.27)$$

$$U_{itn\varepsilon} \leq M \cdot Y_{itn\varepsilon} \qquad \forall i,t,n,\varepsilon \qquad (2.28)$$

$$M \cdot \left(1 - Y_{it(n-1)\varepsilon}\right) \geq I_{itn\varepsilon} - U_{itn\varepsilon} \qquad \forall i,t,n = 3,5,\varepsilon \qquad (2.29)$$

$$Y_{itn\varepsilon} \geq Y_{it(n-1)\varepsilon} \qquad \forall i,t,n = 3,5,\varepsilon \qquad (2.30)$$

$$Y_{0tn\varepsilon} \in \{0,1\}, Y_{itn\varepsilon} \in \{0,1\} \qquad (2.31)$$

Constraints (2.25) - (2.27) ensure that the FIFO issuing policy is applied at the blood center. Platelets at a specific age in the inventory of the blood center can only be allocated to hospitals when remaining inventory for older units is equal to zero. Constraints (2.28) - (2.30) guarantee that the FIFO issuing policy is applied at hospitals. For each demand type, younger units cannot be used to satisfy demand if older units are still available. Constraint (2.31) shows that $Y_{0tn\varepsilon}$ and $Y_{itn\varepsilon}$ are binary variables.

Interestingly, for the stochastic model under the FIFO policy, we obtain the same optimal production cost, inventory holding cost, shortage cost and outdate cost as shown in Table 8. The total transportation cost is only $1 higher than the original model. We can say we get the same performance for both models as the differences of the performance measurements are negligible. Furthermore, we tested both models with different initial inventory levels and we found that wastage was the same for both models. This indicates that an optimal solution need not follow a FIFO policy, but that a FIFO policy can still lead to an optimal (or near optimal) solution.

#### *2.5.3.2. Impact of available platelet donors on different costs*

The number of available platelet donors at hospitals will directly influence the quantity of platelets collected by hospitals, thus leading to changes in performance for the whole network. Total cost, shortage cost, and production cost are three performance measurements used to compare the situations where maximum available platelet donors are 1 to 8, respectively. As

shown in Figure 9, with an increase in the number of available donors at hospitals, costs decrease dramatically especially for shortage costs, while at the same time production cost only increases a little. This trend continues till the number of available donors reaches 6. When the maximum available donors at hospitals is equal or larger than 6, the supply chain performance is optimal and shortage cost is close to zero. This result indicates that recruiting more donors at hospitals is a promising strategy for reducing costs, especially shortage costs, within the platelet supply chain. A minimum of 6 donors should be recruited to attain an optimal performance.

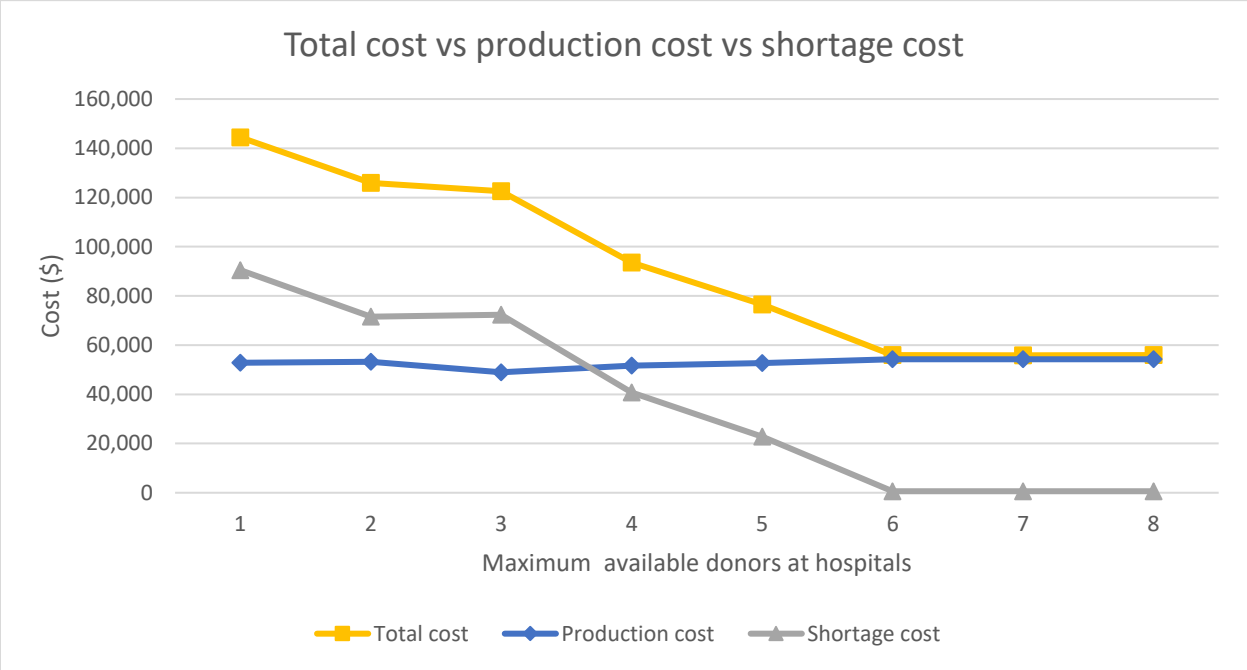


**Figure 9. Result of costs with different maximum available donors at hospitals**

### *2.5.3.3. Impact of capacity level on total cost*

Figure 10 shows the result of total cost with different capacity levels at the blood center. When the capacity level at the blood center is between 20 to 60 units, total cost decreases dramatically as capacity level increases. While when the capacity level is between 60 to 90 units, total cost for the blood supply chain just decreases a little bit which could be negligible. When

the capacity level is larger than 90 units, total cost remains the same. The capacity level has a negative impact on total operational cost in the integrated platelet supply chain. To attain the lowest possible cost, a minimum capacity level of 60 units at the blood center should be maintained.

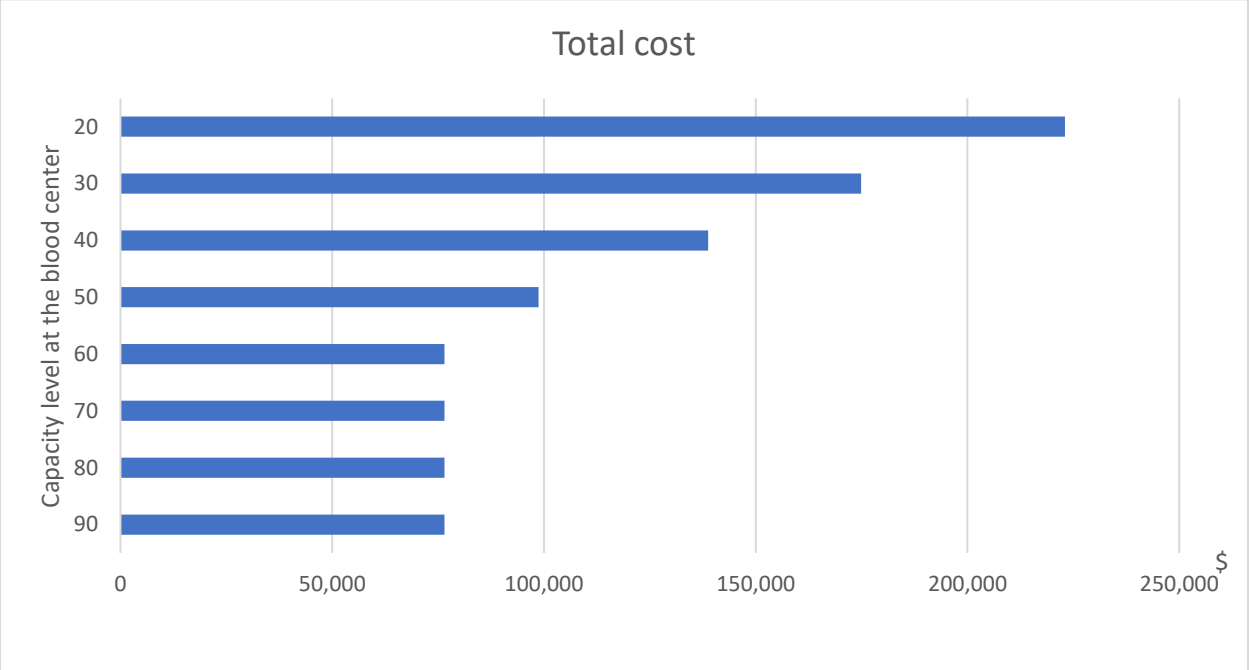


**Figure 10. Result of total cost with different capacity levels at the blood center**

## 2.6. Conclusion

In this study, we developed a stochastic mixed integer program for the integrated platelet supply chain considering multiple sources of supply, age-differentiated demand, and stock age information. The main purpose is to provide tactical and operational decisions on the amount of blood units required to be collected from donors, the amount of platelet units to be produced, and the assignment of platelet units to hospitals. The multi-stage stochastic program was applied to deal with demand uncertainties for hospitals on different days. To demonstrate applications of the proposed model, we presented a real-world platelet supply chain which consists of 3

collection facilities and one regional blood center which provide platelets for 5 registered hospitals in the Fargo-Moorhead area. Our numerical results indicate that platelets collected by apheresis is actually more cost effective than those derived from whole blood, and both the number of available donors and capacity level have negative impacts on total operational cost. These results suggest that hospitals should recruit more platelet donors and the blood center should maintain a minimum capacity level of 60 units. We also observed that it is not necessary for researchers to enforce constraints regarding following a FIFO issuing policy to achieve an optimal performance when optimizing the platelet supply chain.

Several research directions seem promising at this point. First, the consideration of enforcing additional constraints such as maintaining a high service level. Another extension of the present research would be to incorporate new decision variables to find the optimal safety stock in blood centers and hospitals. Finally, a larger supply chain with multiple blood centers competing and cooperating with each other could be considered.

# CHAPTER 3. MODELING THE BENEFITS OF TRANSSHIPMENT WITHIN AN INTEGRATED PLATELET SUPPLY CHIAN NETWORK

## 3.1. Abstract

This paper studies the impact of transshipment between hospitals on performance improvement for a multi-echelon platelet supply chain including collection, production, inventory and distribution. A multi-stage stochastic program considering platelet transshipment and demand uncertainty is developed to minimize total operational cost under centralized control. Applicability of the model is tested through a real-world platelet supply chain with one blood center, three collection facilities, and five hospitals. The proposed model is shown to be good at handling random demand. Our results also indicate that transshipment is useful to reduce shortage and rebalance stock at hospitals so as to improve system cost efficiency, this is particularly beneficial when supply is short. They also suggest that the solution efficiency is sensitive to capacity at the blood center.

## 3.2. Introduction

Despite the significant advancements that have been made in healthcare, blood still plays an irreplaceable role in fulfilling clinical transfusion demand. A shortage of blood can cause incalculable loss to the health and life of people. The fact that blood can only come from human donation makes it a scarce and precious resource. As a result, blood products, such as red blood cells, platelets, and plasma, are always quite expensive and any outdates are undesirable. The highly perishable characteristic of blood adds more complexity to blood supply chain management as balancing shortage and outdating rates is even more challenging. In an empirical study conducted in the state of New South Wales, Australia, Abbasi et al. (2017) emphasized that transshipments are effective for enhancing blood supply chain performance as they observed that

the shortage rate was higher in larger hospitals while outdate rate was higher in smaller hospitals. Yates et al. (2017) also pointed out that one viable approach to minimize shortage and wastage in the blood supply chain is stock sharing or lateral transshipment of blood units close to expiry between hospitals. Intrigued by these studies, we consider transshipment as a good way to optimize the blood supply chain.

The blood supply chain includes four echelons: collection, production, inventory and distribution. In a traditional hierarchical supply chain system, transportation only flows from one echelon to the next, i.e. from blood collection sites to blood centers where production is conducted and from blood centers to hospitals for transfusion. In a more flexible system, transportation flows between organizations in the same echelon are also allowed and this type of flow is referred to lateral transshipment or transshipment, i.e. between blood centers or between hospitals. Transshipment is an efficient strategy that is applied to lower system costs whilst still maintaining the required service level (Paterson et al., 2011). Wang and Ma (2015) demonstrated that transshipment had already been applied to adjust the inbalance between demand and inventory among blood banks in several disasters such as the 9/11 event, SARS, and earthquakes. Although a few researchers have observed that transshipment brought significant reduction in outdate and shortage rates in blood supply chain management, there is a gap in the literature on incorporating transshipment into a mathematical model to optimize and measure the specific impacts of transshipment on wastage and total operational cost.

Our study is motivated by a BloodMove Platelets project conducted throughout regional South Australia where a significant reduction in platelet wastage due to expiry was attained by transshipment between hospitals (National Blood Authority, 2016). The core strategy of the project was establishing a common shared Platelet Expiry Listing showing near expiry platelets

and transferring these units from low to high usage sites. Platelets are the most perishable blood products with a shelf life of five days (American Red Cross, 2017a). They are widely used in today's therapies which include bone marrow transplants, organ transplants, chemotherapy, and radiation treatments (Duan & Liao, 2013). Because of the highly perishable and lifesaving characteristics of platelets, investigating the platelet supply chain with transshipment is extremely challenging and meaningful.

In this paper, we develop a novel multi-stage stochastic program for an integrated platelet supply chain by considering transshipment between hospitals. The proposed model decides the quantity of blood and platelets collected, the quantity of platelets produced, the quantity of platelets delivered, and the quantity of transshipments under different demand scenarios. The objective is to minimize total cost, including production, transportation, transshipment, inventory, shortage and outdate costs, under a centralized control system where centralized decisions on production and replenishment are made with a system-wide perspective. The model is applied to a real-world platelet supply chain in the Fargo-Moorhead area which locates in North Dakota and Minnesota, USA. Impacts of transshipment, available donors at hospitals, and capacity level at the blood center are examined on improving potential performance in the supply chain.

### 3.3. Literature review

We present the related literature in three portions: lateral transshipment, blood supply chain, and transshipment in the blood supply chain. Transshipment, also referred to as stock rotation, lateral transshipment, and inventory pooling, is an important tool that can help improve the performance of an inventory system and supply chain. Paterson et al. (2011) provided a comprehensive review of literature on inventory models regarding lateral transshipment. Based

on the timing of transshipment, they categorized previous research into two main streams: proactive transshipment and reactive transshipment. In proactive transshipment, transshipment occurs at predetermined points in time before demand realization. While, in reactive transshipment, it can take place at any time after observing demand. In this study, we implement a combined proactive and reactive transshipment approach in our multi-stage stochastic model.

A considerable amount of research has been dedicated to lateral transshipments. The majority of transshipment models consider reactive transshipments which are more suitable in a spare parts environment (Patriarca et al., 2016; Yao et al., 2016; Yang et al., 2013). For the proactive transshipment, Meissner and Senicheva (2018) developed a mathematical model for a multi-location inventory system to find an optimal proactive transshipment policy that can maximize the profit of the whole network. Firouz et al. (2017) considered an integrated supplier selection and inventory problem and used a decomposition based heuristic algorithm as well as simulation to investigate the impacts of multi-sourcing and proactive transshipments. There are also some other studies that combine proactive and reactive transshipments, such as Seidscher and Minner (2013) and Glazebrook et al. (2015).

Literature on blood supply chain management dates back to the 1970s and 1980s (Jennings, 1973; Cohen, 1979; Kendall & Lee, 1980; Prastacos, 1984). Beliën and Forcé (2012) and Osorio et al. (2015) presented two recent reviews for supply chain management and inventory models based on different blood products and supply chain echelons, respectively. For supply chain management of platelets, an important thing is to consider age distribution of inventory (Blake 2009). Thus, most recent studies on platelets consider age-based supply chain or inventory models (Abdulwahab & Wahab, 2014; Duan & Liao, 2013, 2014; Ensafian & Yaghoubi, 2017; Ensafian et al., 2017; Gunpinar & Centeno, 2015; Wang & Ma, 2015). In

addition, the reader is referred to Xu and Szmerekovsky (2019), and Ensafian & Yaghoubi (2017) as important examples of an integrated platelet supply chain system.

Although transshipment can help reduce wastage and decrease overall operational cost while maintaining high service levels (Stanger et al., 2013), research efforts considering blood transshipment or transshipment for perishables is significantly limited compared to the large body of research on blood supply chain management. There are several barriers when implementing transshipment in practice. The first and foremost requirement is mutual trust between the organizations involved, in addition, successful communication and information transparency as well as a streamlined logistics for physical transfer are necessary (Stanger et al., 2013).

To overcome the abovementioned barriers, Fontaine et al. (2009) demonstrated that developing fair and detailed contracts and business practices may be one solution for building mutual trust. They applied a novel approach by establishing a collaboration between blood centers and several hospitals through consignment and cost-sharing contracts and reported a significant performance improvement for a platelet supply chain after implementation. Gomez et al. (2015) described the implementation of a novel platelet dashboard suite, including a platelet inventory dashboard and a PLT demand dashboard, which monitors and displays both age distribution of inventory and real-time data on patient information. This platelet dashboard suite was shown to reduce platelet outdate rates significantly over the 48-month study period. The dashboard suite helped overcome the barrier of communication and information transparency.

We now review research on blood transshipment or transshipment for perishables. Cheong (2013) presented a multi-location model for perishable products to find optimal replenishment and transshipment decisions under a single-period planning horizon. Dehghani

and Abbasi (2018) introduced an efficient age-based transshipment policy for perishable products to improve supply chain performance in a continuous review inventory system. For the blood supply chain, the idea of transshipment is not new and can date back to Kendall and Lee (1980). However, studies incorporating transshipment into a quantitative model are more recent. Wang and Ma (2015) used an age-based transshipment model to examine the superiority of a first-in-first-transship method during blood shortage. Hosseinifard and Abbasi (2016) studied the impact of inventory centralization at the second echelon (the hospitals) of a two-echelon blood supply chain system and observed significant reduction in outdate and shortage rates. Najafi et al. (2017) developed a bi-objective integer program to manage blood ordering and issuing in a hospital with consideration of demand uncertainty and blood transshipment. They applied a transshipment threshold to ensure that only nearly-outdated units could be transshipped to other hospitals. Jafarkhan and Yaghoubi (2018) developed a robust stochastic optimization model to analyze the flexible and robust inventory-routing of red blood cells under demand and supply uncertainty. They applied a case study of the Tehran Blood Transfusion Service to examine the impacts of transshipment (between hospitals) and substitution on total routing cost.

To the best of our knowledge, there are no studies that explore quantitative formulations of the platelet supply chain by considering transshipment. The cited research on blood transshipment focuses on red blood cells, which have a much longer shelf life compared to platelets. The outdate rate for platelets is usually much higher than red blood cells. Transshipment should play a more important role in dealing with platelets outdating. Therefore, the main contribution of this study is that we present the first multi-stage stochastic program for an integrated platelet supply chain which takes into account transshipment, demand uncertainty, and age information and investigates the benefit of transshipments.

### 3.4. Problem description and model formulation

Platelets are the small colorless cell fragments in blood and are popularly used in clinical therapies. Based on previous studies, Ensafian and Yaghoubi (2017) categorized the demand for platelets into three groups as shown in Table 10. Patients in the first group need organ transplants or bone marrow and they can only use platelets no more than 1 day old (fresh platelets). Patients in the second group are hematology and oncology cases and should be fulfilled with platelets no more than 3 days old (fresh + young platelets). Patients in the third group need general surgery and they can use platelets of any age (fresh + young + old platelets).

**Table 10. Demand group for platelets**

| Demand group | Age | Usage |
|---|---|---|
| Fresh | 1 day old | Organ transplants and bone marrow |
| Young | 2-3 days old | Hematology and oncology |
| Old | 4-5 days old | Traumatology and general surgery |

Platelets can be obtained through whole blood donation and apheresis donation. An apheresis donation can yield more transfusable units which normally equal up to four to six times that of whole blood donations (American Red Cross, 2017b). But apheresis requires an apheresis machine that collects platelets while returning other blood components, such as red blood cells and plasma, back to the donor. Therefore, apheresis derived platelets are only collected at permanent facilities such as blood centers and hospitals, unlike whole blood derived platelets which can also be collected at temporary facilities such as bloodmobiles.

In this section, we consider an integrated platelet supply chain addressing several blood collection facilities, one regional blood center, and several hospitals considering transshipment (Figure 11). Each dotted line represents a flow of transportation. The lateral transshipment between hospitals is bidirectional. Therefore, platelet units can be transferred from a bigger

hospital with higher demand to a smaller hospital with lower demand, and vice versa. Transferring extra platelet units between hospitals can help organizations deal with demand variability and stock outs and lead to a more balanced inventory system. The platelet supply chain starts with blood collection from registered donors at blood collection facilities, the blood center, or hospitals. The whole blood units collected at collection facilities are then sent to the blood center to extract platelets. After processing and testing in the blood center, any platelet that is available for transfusion will be put into inventory for future needs. In the end, platelets stored in the inventory will be distributed to hospitals to fulfill transfusion demand for different groups of patients. Table 11 shows the sequence of daily events at the blood center and hospitals.

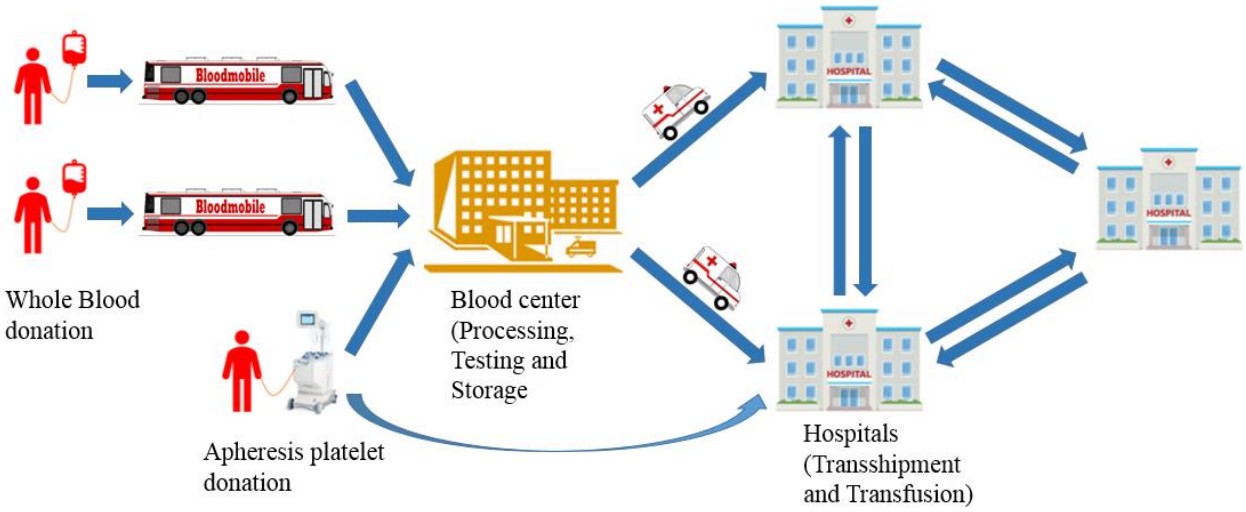


**Figure 11. Platelet supply chain network considering transshipment**

**Table 11. Sequence of daily events at the blood center and hospitals**

| Sequence | Blood center | Hospitals |
|---|---|---|
| 1 | Distribute platelets | Receive platelets |
| 2 | Blood collection and production | Blood transshipment |
| 3 | - | Satisfy demand |
| 4 | Remove outdated units | Remove outdated units |
| 5 | Update inventory status | Update inventory status |
| 6 | Determine production plan | Place order |

Based on the above description, the following assumptions have been considered:

- Two days are needed for processing and testing of whole blood units (Ensafian & Yaghoubi, 2017), while it only takes one day for bacterial testing of apheresis derived platelets according to a manager in a local blood center.
- Lead time for transporting platelets from the blood center to any hospital is zero and doesn't have any effect on the age of delivered units. As we are considering a local area, distance between the blood center and hospitals is relatively small,
- Lead time for platelet transshipment between hospitals is negligible and has no effect on platelet age. The hospitals considered in this study are close to each other.

Since the demand for platelets at hospitals is uncertain and exact information emerges slowly in a multi-period environment, we develop a scenario-based multi-stage stochastic program which is useful in dealing with uncertainty in a dynamic environment (see Birge & Louveaux, 2011). In a multi-stage framework, only the first-stage decisions are independent of generated scenarios and are made before uncertainty is revealed, the decisions in the following stages respond to realized outcomes which are unknown a priori. In this study, the first-stage decisions primarily constitute the supply of whole blood and apheresis derived platelets at the blood center. The second stage decisions mainly include regular operations, such as production, distribution, transshipment, inventory, shortage, and wastage at the blood center and hospitals under each scenario in the first day. The third stage decisions are those referring to the operation of the supply chain on the second day when information for the first day is attained. This process for decision-making repeats till the last day within the planning horizon.

### 2.4.1. Parameters and variables

The following parameters and decision variables are used in the proposed stochastic mathematical model.

**Table 12. Notation used in the platelet supply chain considering transshipment**

| **Sets** | **Description** |
|---|---|
| $T$ | Time periods, $t \in T$ |
| $I$ | Hospitals, $i, m \in I$ |
| $J$ | Blood collection facilities, $j \in J$ |
| $N$ | Platelet age, $n \in N$ |
| $K$ | Demand group for platelets, $k \in K = \{1,3,5\}$ |
| $E$ | Scenarios, $\varepsilon \in$ E |
| | |
| **Parameters** | |
| $F$ | Fixed cost of producing whole blood derived platelets at the blood center |
| $V$ | Variable cost of producing one unit of whole blood derived platelet at the blood center |
| $p$ | Cost of producing one unit of apheresis derived platelet at the blood center and hospitals |
| $H_i$ | Transportation cost of one platelet unit from the blood center to hospital $i$ |
| $G_j$ | Transportation cost of one whole blood unit from collection facility $j$ to the blood center |
| $L_{im}$ | Transshipment cost of one platelet unit from hospital $i$ to hospital $m$ |
| $h$ | Inventory holding cost per unit per day |
| $u$ | Shortage cost per unit |
| $v$ | Outdating cost per unit |
| $W_{jt}$ | The number of whole blood donors on day $t$ at collection facility $j$ |
| $X_{it}$ | The number of platelet donors on day $t$ at hospital $i$ |
| $X_{0t}$ | The number of platelet donors on day $t$ at the blood center |
| $d_{itk\varepsilon}$ | Demand for patients in the $k$ group on day $t$ at hospital $i$ under scenario $\varepsilon$ |
| $D_k$ | Set of platelet ages associated with demand group $k$ |
| $C_0$ | Platelet storage capacity at the blood center |
| $C_i$ | Storage capacity at hospital $i$ |
| $C_i^{Initial}$ | Upper bound for initial inventory capacity at hospital $i$ |
| $N$ | Maximum lifetime of platelets |
| $\theta$ | Proportion of whole blood collected used to extract platelets |
| $\gamma$ | Percentage of whole blood units that are not suitable to produce platelets |
| $\beta$ | The amount of extracted platelet units from a donor by apheresis |
| $P_\varepsilon$ | Probability associated with scenario $\varepsilon$ |
| | |
| **Variables** | |
| $I_{0tn\varepsilon}$ | Inventory level of the blood center for platelets aged $n$ at the beginning of day $t$ under scenario $\varepsilon$ |

**Table 12. Notation used in the platelet supply chain considering transshipment (continued)**

| Variables | Description |
|---|---|
| $I_{itn\varepsilon}$ | Inventory level of hospital $i$ for platelets aged $n$ at the beginning of day $t$ under scenario $\varepsilon$ |
| $U_{itn\varepsilon}$ | Demand realization of platelets aged $n$ in the inventory of hospital $i$ on day $t$ under scenario $\varepsilon$ |
| $Y_{imtn\varepsilon}$ | Quantity of platelets age $n$ transshipped from hospital $i$ to hospital $m$ on day $t$ under scenario $\varepsilon$ |
| $R_{itn\varepsilon}$ | Quantity of platelets aged $n$ received by hospital $i$ on day $t$ under scenario $\varepsilon$ |
| $B_{jt}$ | Quantity of whole blood collected from blood collection facility $j$ on day $t$ |
| $Z_t$ | 1 if platelets are produced from whole blood at the blood center on day $t$, 0 otherwise |
| $Q_t$ | Quantity of platelets extracted from whole blood at the blood center on day $t$ |
| $A_{0t}$ | Quantity of platelet apheresis at the blood center on day $t$ |
| $A_{it}$ | Quantity of platelet apheresis at hospital $i$ on day $t$ |
| $S_{itk\varepsilon}$ | Shortage quantity of platelets for demand group $k$ at hospital $i$ on day $t$ under scenario $\varepsilon$ |
| $O_{0t\varepsilon}$ | Outdated quantity of platelets at the blood center on day $t$ under scenario $\varepsilon$ |
| $O_{it\varepsilon}$ | Outdated quantity of platelets at hospital $i$ on day $t$ under scenario $\varepsilon$ |

### 3.4.2. Mathematical model

We develop a multi-stage stochastic model which includes all echelons of collection, production, inventory and distribution considering transshipment in the platelet supply chain. Two types of platelet collection methods and three types of demand are taken into account. Therefore, in order to minimize the total operational cost of the supply chain, the decisions need to be optimized are: the amount of blood units required to be collected from donors, the amount of platelet units to be produced, the assignment of platelet units to hospitals, and the amount of platelet units to be transshipped between hospitals.

The mixed-integer mathematical model is formulated as follows:

$$\begin{aligned} Min\ & \sum_{t=1}^{T} F * Z_t + \sum_{t=1}^{T} V * Q_t + \sum_{t=1}^{T} p * A_{0t} + \sum_{t=1}^{T}\sum_{i=1}^{N} p * A_{it} + \\ & \sum_{t=1}^{T}\sum_{j=1}^{J} G_j * B_{jt} + \sum_{\varepsilon}\sum_{t=1}^{T}\sum_{i=1}^{I}\sum_{n=1}^{N} P_\varepsilon * H_i * R_{itn\varepsilon} + \\ & \sum_{\varepsilon}\sum_{t=1}^{T}\sum_{i=1}^{I}\sum_{m=1,m\neq i}^{I}\sum_{n=1}^{N} P_\varepsilon * L_{im} * Y_{imtn\varepsilon} + \sum_{\varepsilon}\sum_{t=1}^{T}\sum_{i=1}^{I}\sum_{n=1}^{N} P_\varepsilon * h * I_{itn\varepsilon} + \end{aligned} \quad (3.1)$$

$$\sum_{\varepsilon}\sum_{t=1}^{T}\sum_{n=1}^{N} P_{\varepsilon} * h * I_{0tn\varepsilon} + \sum_{\varepsilon}\sum_{k=1}^{K}\sum_{t=1}^{T}\sum_{i=1}^{I} P_{\varepsilon} * u * S_{itk\varepsilon} + \sum_{\varepsilon}\sum_{t=1}^{T}\sum_{i=1}^{I} P_{\varepsilon} * v * O_{it\varepsilon} + \sum_{\varepsilon}\sum_{t=1}^{T} P_{\varepsilon} * v * O_{0t\varepsilon} + \sum_{\varepsilon}\sum_{n=2}^{N} P_{\varepsilon} * (I_{01n\varepsilon} + \sum_{i=1}^{I} I_{i1n\varepsilon}) * (V + h)$$

s.t.

$$Q_t \leq C_0 * Z_t \qquad \forall t \qquad (3.2)$$

$$\sum_{n=1}^{N-1} I_{0tn\varepsilon} \leq C_0 \qquad \forall t, \varepsilon \qquad (3.3)$$

$$\sum_{n=1}^{N-1} I_{itn\varepsilon} \leq C_i \qquad \forall i, t, \varepsilon \qquad (3.4)$$

$$B_{jt} \leq W_{jt} \qquad \forall j, t \qquad (3.5)$$

$$A_{0t} \leq X_{0t} \qquad \forall t \qquad (3.6)$$

$$A_{it} \leq X_{it} \qquad \forall i, t \qquad (3.7)$$

$$\sum_{j=1}^{J} B_{jt} * \theta * (1 - \gamma) \geq Q_{t+2} \qquad t = 1, \dots, T-2 \qquad (3.8)$$

$$I_{0(t+1)n\varepsilon} = I_{0t(n-1)\varepsilon} - \sum_{i=1}^{I} R_{it(n-1)\varepsilon} \qquad \forall \varepsilon, t = 1, \dots, T-1, n = 3, \dots, N \qquad (3.9)$$

$$I_{0(t+1)2\varepsilon} = I_{0t1\varepsilon} + Q_{t+1} - \sum_{i=1}^{I} R_{it1\varepsilon} \qquad \forall \varepsilon, t = 1, \dots, T-1 \qquad (3.10)$$

$$I_{0t1\varepsilon} \geq \sum_{i=1}^{I} R_{it1\varepsilon} \qquad \forall \varepsilon, t \qquad (3.11)$$

$$I_{0(t+1)1\varepsilon} = \beta * A_{0t} \qquad t = 1, \dots, T-1 \qquad (3.12)$$

$$I_{i(t+1)1\varepsilon} = \beta * A_{it} \qquad \forall \varepsilon, i, t = 1, \dots, T-1 \qquad (3.13)$$

$$I_{i(t+1)n\varepsilon} = I_{it(n-1)\varepsilon} + R_{it(n-1)\varepsilon} + \sum_{m=1}^{I} Y_{mit(n-1)\varepsilon} - \sum_{m=1}^{I} Y_{imt(n-1)\varepsilon} - U_{it(n-1)\varepsilon}$$
$$\forall \varepsilon, i, m, i \neq m, t = 1, \dots, T-1, n = 2, \dots, N \qquad (3.14)$$

$$U_{it1\varepsilon} + \sum_{m=1}^{I} Y_{mit1\varepsilon} - \sum_{m=1}^{I} Y_{imt1\varepsilon} + S_{it1\varepsilon} \geq d_{it1\varepsilon} \qquad \forall \varepsilon, i, m, i \neq m, t \qquad (3.15)$$

$$\sum_{n=1}^{3} U_{itn\varepsilon} + \sum_{n=1}^{3}\sum_{m=1}^{I} Y_{mitn\varepsilon} - \sum_{n=1}^{3}\sum_{m=1}^{I} Y_{imtn\varepsilon} + S_{it1\varepsilon} + S_{it3\varepsilon} \geq d_{it1\varepsilon} + d_{it3\varepsilon} \qquad \forall \varepsilon, i, m, i \neq m, t \qquad (3.16)$$

$$\sum_{n=1}^{5} U_{itn\varepsilon} + \sum_{n=1}^{5}\sum_{m=1}^{I} Y_{mitn\varepsilon} - \sum_{n=1}^{5}\sum_{m=1}^{I} Y_{imtn\varepsilon} + S_{it1\varepsilon} + S_{it3\varepsilon} + S_{it5\varepsilon} \geq d_{it1\varepsilon} + d_{it3\varepsilon} + d_{it5\varepsilon} \qquad \forall \varepsilon, i, m, i \neq m, t \qquad (3.17)$$

$$\sum_{m=1}^{I} Y_{imtn\varepsilon} \leq I_{itn\varepsilon} + R_{itn\varepsilon} \qquad \forall \varepsilon, i, m, i \neq m, t, n \qquad (3.18)$$

$$I_{itn\varepsilon} = O_{it\varepsilon} \qquad \forall \varepsilon, i, t, n = N \tag{3.19}$$

$$I_{0tn\varepsilon} = O_{0t\varepsilon} \qquad \forall \varepsilon, i, t, n = N \tag{3.20}$$

$$Q_2 = 0 \tag{3.21}$$

$$\sum_{n=1}^{N-1} I_{01n\varepsilon} \leq \sum_{i=1}^{I} C_i^{Initial} \qquad \forall \varepsilon \tag{3.22}$$

$$\sum_{n=1}^{N-1} I_{i1n\varepsilon} \leq C_i^{Initial} \qquad \forall i, \varepsilon \tag{3.23}$$

$$B_{jt}, Q_t, A_{it}, A_{0t}, O_{it\varepsilon}, O_{0t\varepsilon}, I_{itn\varepsilon}, I_{0tn\varepsilon}, S_{itk\varepsilon}, R_{itn\varepsilon}, U_{itn\varepsilon} \geq 0 \tag{3.24}$$

$$Z_t \in \{0,1\} \tag{3.25}$$

The total operational cost is minimized by objective function (3.1). This cost includes production cost of whole blood derived platelets at the blood center and apheresis derived platelets at both the blood center and hospitals, transportation cost of whole blood from collection facilities to the blood center and platelets from the blood center to hospitals, transshipment cost of platelets between hospitals, inventory holding cost at the blood center and hospitals, outdate cost at the blood center and hospitals, shortage cost at hospitals and cost for initial inventory at both the blood center and hospitals. Transshipment cost includes any cost incurred for transporting platelets from one hospital to another one, either those transported platelets are produced at the former hospital or at the blood center. An outdate cost is incurred if any platelet in the inventory is expired and a shortage cost is incurred if demand is not fully satisfied. Initial inventory cost is estimated to be unit production cost plus additional one-day holding cost.

Constraints (3.2) and (3.3) put upper limits for the platelet production and storage capacity of the blood center on each day. Constraint (3.4) is the storage capacity constraint of each hospital on each day under each scenario. Constraints (3.5) - (3.7) put upper bounds on the

number of whole blood donations and apheresis platelet donations, respectively. Constraint (3.8) is the balance constraint for whole blood donated and platelets extracted considering two days needed for processing and testing. The parameter $\gamma$ is incorporated to represent the proportion of whole blood collected which is not appropriate for platelet production as some units are not rich enough to extract platelets. Constraints (3.9) – (3.12) are inventory balance constraints which update platelet inventory levels at the blood center at the start of each day based on age groups. Constraint (3.9) shows that the inventory level of platelets more than two days old is equal to the inventory level of the previous day minus the total quantity delivered to hospitals in the previous day. Constraint (3.10) states that two-day-old inventory is given by the previous inventory level, the quantity of platelets produced from whole blood, and the quantity of platelets distributed to hospitals in the previous period. Constraint (3.11) enforces that the number of platelets delivered cannot exceed the inventory level of the blood center. Constraint (3.12) updates the status of one-day-old inventory. Because one day is required for testing apheresis derived platelets, they are assigned to the one-day-old inventory.

Constraints (3.13) and (3.14) are inventory balance constraints which update platelet inventory levels at hospitals at the start of each day for each age group. Constraint (3.13) shows that one-day-old inventory at hospitals equals the quantity of apheresis derived platelets collected in the previous day. Constraint (3.14) shows that the inventory level of platelets more than one day old is given by the previous inventory level, the quantity of platelets received from the blood center, the total quantity of platelets transshipped from other hospitals, the total quantity of platelets transshipped to other hospitals, and the quantity used to fulfill demand in the previous day. Constraints (3.15) – (3.17) capture the shortage quantity for fresh, young, and old platelets at hospitals on each day, respectively. Note that fresh platelets are suitable to be transfused to

patients in any demand group and young platelets can be transfused to patients requiring young or old platelets. Constraint (3.18) ensures that the quantity of platelets transshipped from one hospital does not exceed the amount available in its age group for the given hospital on each day. Constraints (3.19) and (3.20) identify the number of outdated platelets on each day at hospitals and the blood center, respectively. Constraint (3.21) guarantees that there are no whole blood derived platelets on the second day. Constraints (3.22) and (3.23) set upper bounds for the initial inventory at the blood center and hospitals, respectively. Constraints (3.24) and (3.25) define the domains of all decision variables.

## 3.5. Computational study

### 3.5.1. Case description

We present a case study for a real-world platelet supply chain in the Fargo-Moorhead area. The Fargo-Moorhead area comprises Fargo, ND, Moorhead, MN, and the surrounding cities in the USA. The instances involve three blood collection sites, one blood center, and five hospitals in the local area within a six-day planning horizon. Figure 12 shows the geographical locations of the blood center, collection facilities, and hospitals in Fargo and Moorhead. A total of 32 demand scenarios are generated with equal probability $P_\varepsilon$ of 1/32. The data used to valuate the mathematical model is presented as follows.

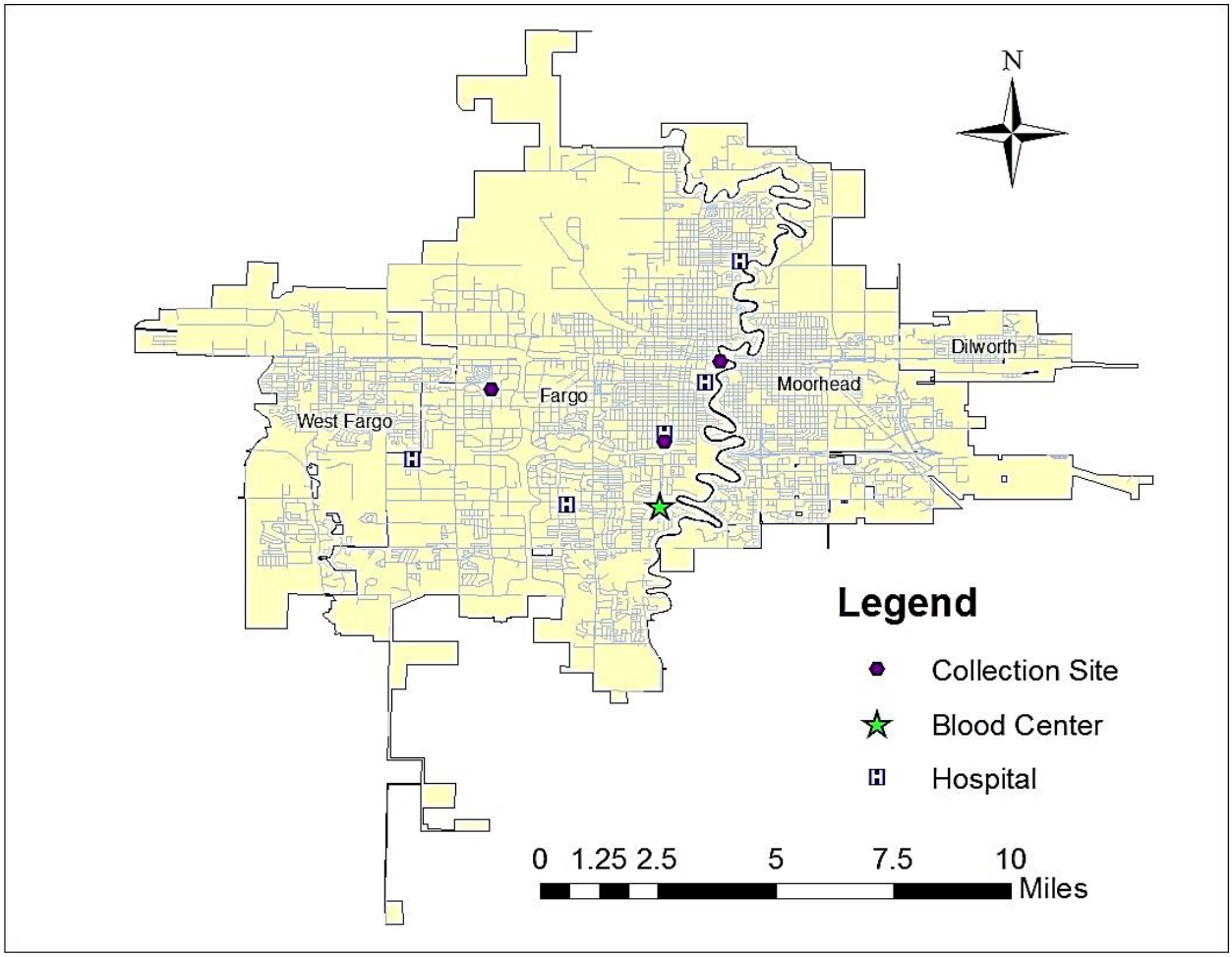


**Figure 12. The geographical locations of collection sites, the blood center, and hospitals in the Fargo-Moorhead area**

#### *3.5.1.1. Demand*

The platelet demand on each day for each hospital is assumed to follow a Poisson distribution and to be independent of each other. Based on previous research by Ensafian and Yaghoubi (2017) and Haijema et al. (2007), the mean values of daily demand at a regular hospital with around 100-150 beds within a six-day time horizon are: 24, 16, 32, 16, 24, and 8, respectively. We assign a demand coefficient to each considered hospital to estimate its mean daily demand based on the number of hospital beds. The resulting mean daily demand at each

hospital on each day is shown in Table 13. The demand for fresh, young and old platelets is estimated to be a proportion of total demand. We adapted 20% for fresh, 50% for young, and 30% for old platelets according to Haijema et al. (2007).

**Table 13. Mean daily demand at each hospital on each day**

| Days | Hospital 1 | Hospital 2 | Hospital 3 | Hospital 4 | Hospital 5 |
|---|---|---|---|---|---|
| 1 | 18 | 42 | 24 | 12 | 24 |
| 2 | 12 | 28 | 16 | 8 | 16 |
| 3 | 24 | 56 | 32 | 16 | 32 |
| 4 | 12 | 28 | 16 | 8 | 16 |
| 5 | 18 | 42 | 24 | 12 | 24 |

To deal with demand uncertainty in a dynamic environment, we generated two scenarios on each day, a total of 32 scenarios within the six-day planning period. For each day, demand for each hospital is generated from its relevant Poisson distribution with mean value shown in Table 13. Note that 32 demand scenarios doesn't mean we generate 32 random numbers for demand on each day. Instead, we generate two random numbers using MATLAB on each day, but with the combination of demand on other days, we get 32 different demand scenarios. To reflect this scenario generation process in our multi-stage stochastic program, we adopt the scenario tree structure from Xu and Szmerekovsky (2019) as shown in Figure 13. This is a five-stage scenario tree with 63 nodes and 32 scenarios. Different nodes denote different demand levels and different arcs denote different demand combinations within the planning horizon. Note that non-anticipativity constraints must be added for a multi-stage formulation. This means that the value of a decision variable in the current period should be the same if it has the same historical information. In this study, we have one type of decision variable that must satisfy the non-anticipativity constraints, the quantity of platelets received by hospitals each day under each scenario ($R_{itn\varepsilon}$). These non-anticipativity constraints are also shown in Figure 13. For example,

“R217=R218=…=R223=R224” means that the quantities of platelets in each age group received by each hospital on the second day are the same for scenarios 17-24.

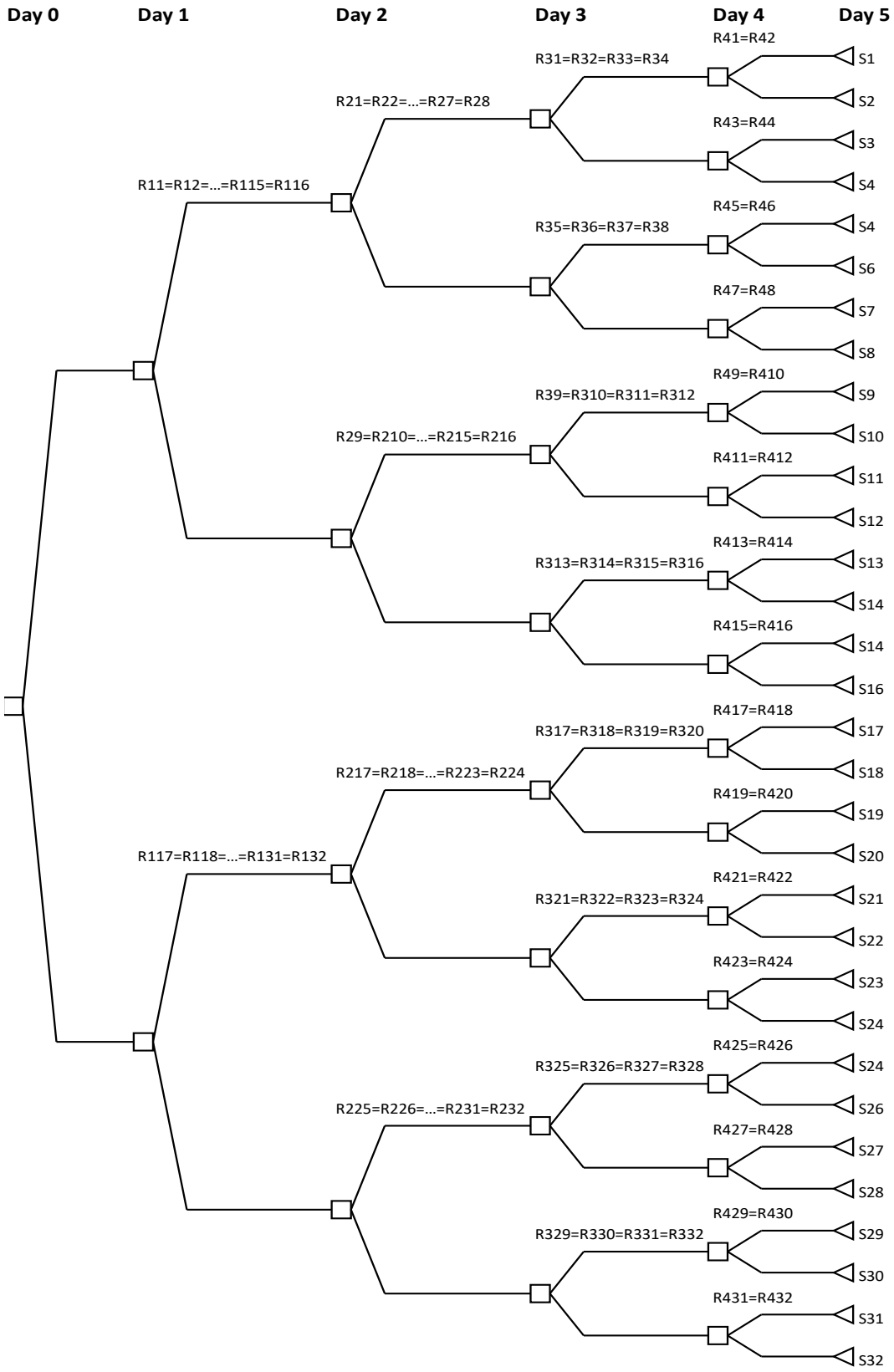


**Figure 13. A schematic view of the scenario tree for demand**

#### *3.5.1.2. Supply*

Platelets can come from apheresis donation at the blood center and hospitals as well as whole blood donation at collection facilities. Therefore, the upper bound for platelet supply depends on the number of relevant donors at these three locations. According to real data collected for available appointments at different sites under a four-month period, we assume that the number of available donors on each day follows uniform distributions as depicted in Table 14.

**Table 14. Number of available donors**

| Type of donors | Value (unit) |
|---|---|
| Whole blood donors at collection sites | Uniform ~ [15,25] |
| Apheresis platelet donors at the blood center | Uniform ~ [10,15] |
| Apheresis platelet donors at hospitals | Uniform ~ [0,5] |

#### *3.5.1.3. Cost settings*

The fixed and variable production costs of extracting platelets from whole blood are obtained from Ensafian and Yaghoubi (2017). The production cost of apheresis derived platelets is taken from Barbee et al. (2015). The inventory holding, shortage, and outdating costs are from Gunpinar and Centeno (2015). Table 15 summarizes these cost parameters, while the values of transportation and transshipment costs are shown in Tables 16 and 17. Table 16 shows the unit costs of transporting whole blood from each collection facility to the blood center and transferring platelets from the blood center to each hospital. Table 17 presents the unit cost of transshipping platelets from one hospital to another one. Both costs are assumed to be proportional to the geographical distance with a unit shipping cost of $0.19 per mile (Ensafian & Yaghoubi, 2017).

**Table 15. Cost parameters**

| Cost parameter | Value | Units |
|---|---|---|
| Fixed production cost | 1 | $/unit |
| Variable production cost | 150 | $/unit |
| Apheresis production cost | 538 | $/unit |
| Inventory holding cost | 1.25 | $/unit |
| Shortage cost | 1500 | $/unit |
| Outdating cost | 150 | $/unit |

**Table 16. Transportation cost from/to the blood center ($/unit)**

| Location | Value |
|---|---|
| Collection facility 1 | 0.94 |
| Collection facility 2 | 0.85 |
| Collection facility 3 | 0.25 |
| Hospital 1 | 1.19 |
| Hospital 2 | 0.88 |
| Hospital 3 | 0.63 |
| Hospital 4 | 0.32 |
| Hospital 5 | 0.31 |

**Table 17. Transshipment cost between hospitals ($/unit)**

| Location | Hospital 1 | Hospital 2 | Hospital 3 | Hospital 4 | Hospital 5 |
|---|---|---|---|---|---|
| Hospital 1 | - | - | - | - | - |
| Hospital 2 | 1.75 | - | - | - | - |
| Hospital 3 | 0.58 | 1.15 | - | - | - |
| Hospital 4 | 0.92 | 0.83 | 0.33 | - | - |
| Hospital 5 | 1.46 | 0.60 | 0.87 | 0.54 | - |

#### *3.5.1.4. Other input parameters*

We assume that all the whole blood units collected are used for producing platelets, so $\theta$ = 1. For the percentage of inappropriate whole blood units, we adopt the value of 2% for $\gamma$ in accordance with Ensafian and Yaghoubi (2017). $\beta$ is considered as 5 which means that the

amount of extracted platelet units from a donor by apheresis procedure is five times of a single whole blood donation (American Red Cross, 2017b).

### 3.5.2. Numerical results

The stochastic program is solved using IBM ILOG CPLEX 12.8 on Dell OPTIPLEX 9020 computer running with 3.40 GHz CPU and 16GB of RAM. The proposed model has 24,615 constraints and 51,522 variables with 32 demand scenarios.

In an integrated platelet supply chain system, the total operational cost involves production, transportation, transshipment, inventory holding, and initial inventory as well as penalty costs for shortage and outdates. Table 18 shows a summary of the numerical results for these different types of costs in the planning period. The total operational cost for the time period is $77,653. Production cost takes the largest proportion, approximately 87.48%, and this is due to the high unit production cost of platelets. This cost includes production cost for initial inventory and platelet production within the six-day planning horizon. The quantity of platelets produced on average is around 453 units for all scenarios. And the average initial inventory is about 58 units at hospitals and 60 units at the blood center. Shortage cost takes the second largest proportion, about 11.11%. Some shortage occurs on the first day and some on the third day. If initial inventory can't guarantee the demand on the first day, shortage occurs since platelet production will take at least one day. The inventory holding cost takes the third largest proportion with 1.22%. Note that the additional one day holding cost for initial inventory is combined into the total inventory holding cost. The total quantity of platelet inventory is approximately 639 units on average under all scenarios. Transportation and transshipment costs are relatively small compared with other types of costs. This is reasonable as we are considering a local area where distance between any two locations of the blood center, collection facilities, or

hospitals is relatively small. The costs on the sixth day are close to zero as no demand is considered on the last day. Outdate costs are zero and are thus not shown in the table.

**Table 18. Results for daily cost**

| | Total cost | Production cost | Transportation cost | Holding cost | Transshipment cost | Shortage cost |
|---|---|---|---|---|---|---|
| **Day 1** | 33,627 | 29,536 | 34 | 295 | 12 | 3,750 |
| **Day 2** | 11,464 | 11,298 | 16 | 140 | 10 | 0 |
| **Day 3** | 19,755 | 14,611 | 27 | 223 | 19 | 4,875 |
| **Day 4** | 12,617 | 12,482 | 8 | 119 | 9 | 0 |
| **Day 5** | 178 | 0 | 10 | 157 | 11 | 0 |
| **Day 6** | 12 | 0 | 0 | 12 | 0 | 0 |
| **Total** | 77,653 | 67,927 | 95 | 947 | 60 | 8,625 |

As a good strategy of improving the supply chain, lateral transshipment between hospitals can help deal with demand and supply uncertainty. Figure 14 shows the total number of platelets transshipped under each scenario for the proposed model. As we can see, the quantity of transshipment ranges from 110 to 130 units. The maximum number of transshipped platelets is 126 units under scenarios 19 and 20. The total number of platelets transshipped between hospitals in the planning horizon is depicted in Table 19. The value shown in the table is not integer because we are using the average number of 32 scenarios. There are about 117.56 units of platelets transshipped between hospitals. Most transshipments take place from hospitals 5 to 2, and the quantity of transshipped platelets is 59.06 units. This is expected as demand for hospital 2 is the highest. The second largest number of transshipped platelets is from hospital 4 to hospital 3. Transshipment between hospitals 1 and 3 is bidirectional, but it does not occur in both directions on the same day. Table 20 shows the number of platelets transshipped from each hospital for each age group. All ages of platelets are transshipped, while most transshipped platelets are fresh ones. Transshipment plays an important role in inventory reallocation for the proposed model.

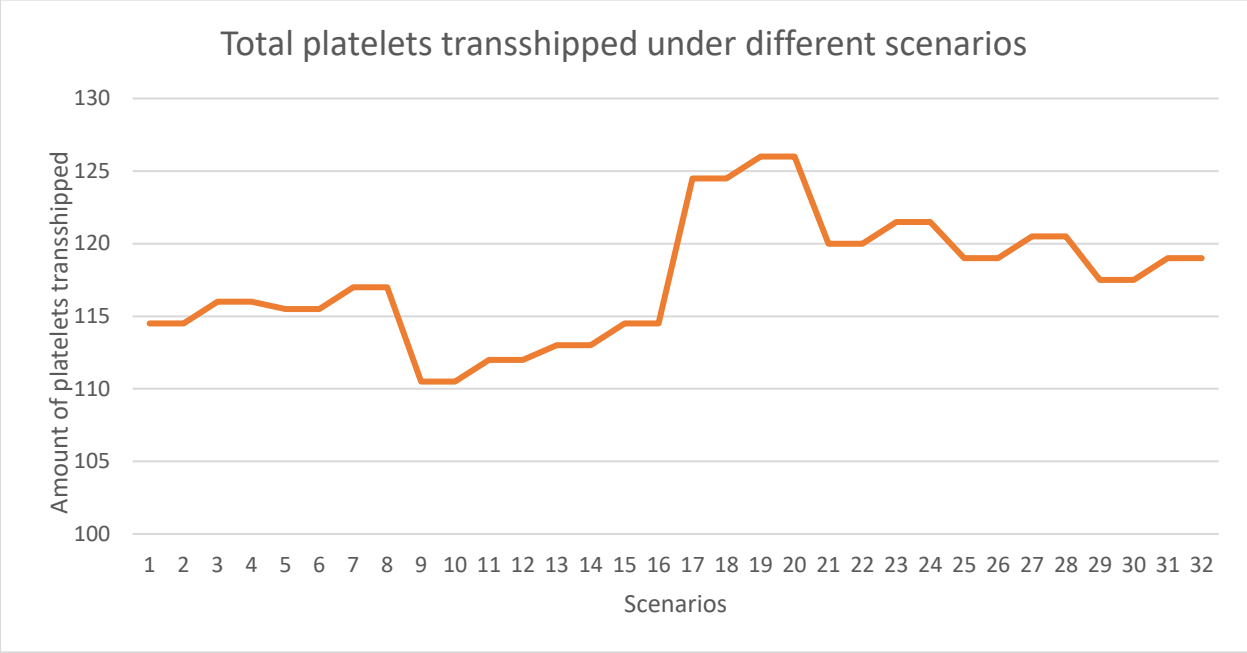


**Figure 14. Result of blood transshipment under different scenarios**

**Table 19. The total number of platelets transshipped between hospitals**

| **Location** | Hospital 1 | Hospital 2 | Hospital 3 | Hospital 4 | Hospital 5 |
|---|---|---|---|---|---|
| Hospital 1 | - | 0 | 2.75 | 0 | 0 |
| Hospital 2 | 0 | - | 0 | 0 | 0 |
| Hospital 3 | 12.94 | 0 | - | 0 | 0 |
| Hospital 4 | 0 | 3.38 | 39.44 | - | 0 |
| Hospital 5 | 0 | 59.06 | 0 | 0 | - |

**Table 20. The number of platelets transshipped from each hospital in each age group**

| | **Age 1** | **Age 2** | **Age 3** | **Age 4** | **Age 5** |
|---|---|---|---|---|---|
| Hospital 1 | 2.75 | 0.00 | 0.00 | 0.00 | 0.00 |
| Hospital 2 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Hospital 3 | 9.47 | 1.64 | 0.69 | 0.69 | 0.45 |
| Hospital 4 | 29.06 | 7.57 | 3.11 | 2.12 | 0.95 |
| Hospital 5 | 29.29 | 18.67 | 5.27 | 1.99 | 3.84 |
| Total | 70.57 | 27.88 | 9.07 | 4.80 | 5.24 |

### 3.5.3. Impact of transshipment on system performance

The proposed model is compared with a model that doesn't consider transshipment between hospitals to evaluate the impact of transshipment on system performance. Total cost, inventory holding cost, production cost, transportation cost, and initial inventory cost are performance measurements. Fifteen groups of data are randomly generated from the mean demand listed in Table 13 to conduct experiments. A paired sample T-test is conducted to compare the total costs for both models. Our result shows that there is a statistically significant difference between the means of total cost for both models (p-value = 0.000 < 0.05).

Comparisons of the model with transshipment and the model without transshipment are shown in Table 21, where the results are the averages from 15 experiments. The total cost for the model without transshipment is about $85,073, an increase of 8.50% compared to the model with transshipment. The increase in total cost mainly comes from increased shortage cost. The quantity of shortage on average is 11.5 units for the model without transshipment compared to 6.7 units for the model with transshipment, nearly double. The production cost and inventory holding cost decrease for the model without transshipment. The average quantity of production including initial inventory is 560 units for the model without transshipment and is 567 units for the model with transshipment. The difference between the productions is approximately equal to the quantity of shortage. As demand for both models is the same and no outdates occur, additional platelet production is needed to satisfy extra demand for the model with transshipment to avoid shortage. Transshipment also helps in reducing transportation cost between the blood center and hospitals. From these results, we can conclude that transshipment plays an important role in alleviating shortage and balancing inventory at different hospitals for the platelet supply chain.

**Table 21. Comparisons of different costs for models with and without transshipment**

| | With transshipment | Without transshipment | Change |
|---|---|---|---|
| **Production cost** | 67,201.07 | 66,699.17 | -0.75% |
| **Holding cost** | 942.43 | 917.72 | -2.62% |
| **Shortage cost** | 10,112.50 | 17,237.50 | 70.46% |
| **Transportation cost** | 87.81 | 218.66 | 149.02% |
| **Transshipment cost** | 63.28 | - | - |
| **Total cost** | 78,407.09 | 85,073.05 | 8.50% |

### 3.5.4. Sensitivity analysis

In this section, we perform sensitivity analysis to explore the impacts of available platelet donors at hospitals and capacity levels at the blood center on different costs. In addition, the impact of transshipment is also considered for both analyses.

#### *3.5.4.1. Impact of available platelet donors on costs*

As minimizing total cost is the main focus of the integrated platelet supply chain, and production cost and shortage cost constitute over 95% of total cost, these three costs are main indicators to assess the performance of the system. Figure 15 shows the average result of total cost, production cost, and shortage cost with different maximum number of available donors at each hospital with 15 replications for each number. As we have defined the number of available platelet donors at hospitals on each day to follow a uniform distribution with lower bound of 0 and upper bound of 5, the number of maximum available donors is 5 at each hospital for our base case. When the maximum number of available donors increases from 1 to 8, shortage cost decreases dramatically, so does total cost as the increase in production cost is negligible. This can be explained by the fact that a larger number of available platelet donors will result in collecting more units of platelets daily and thus decrease the shortage quantity. When the maximum number of available donors is 6 or above, the platelet supply chain achieves a

minimum total cost and the shortage cost is almost zero. From this result, a potential strategy to improve the supply chain performance is by recruiting more donors at hospitals. In our example, it is enough to recruit 6 donors in order to achieve the majority of the benefits.

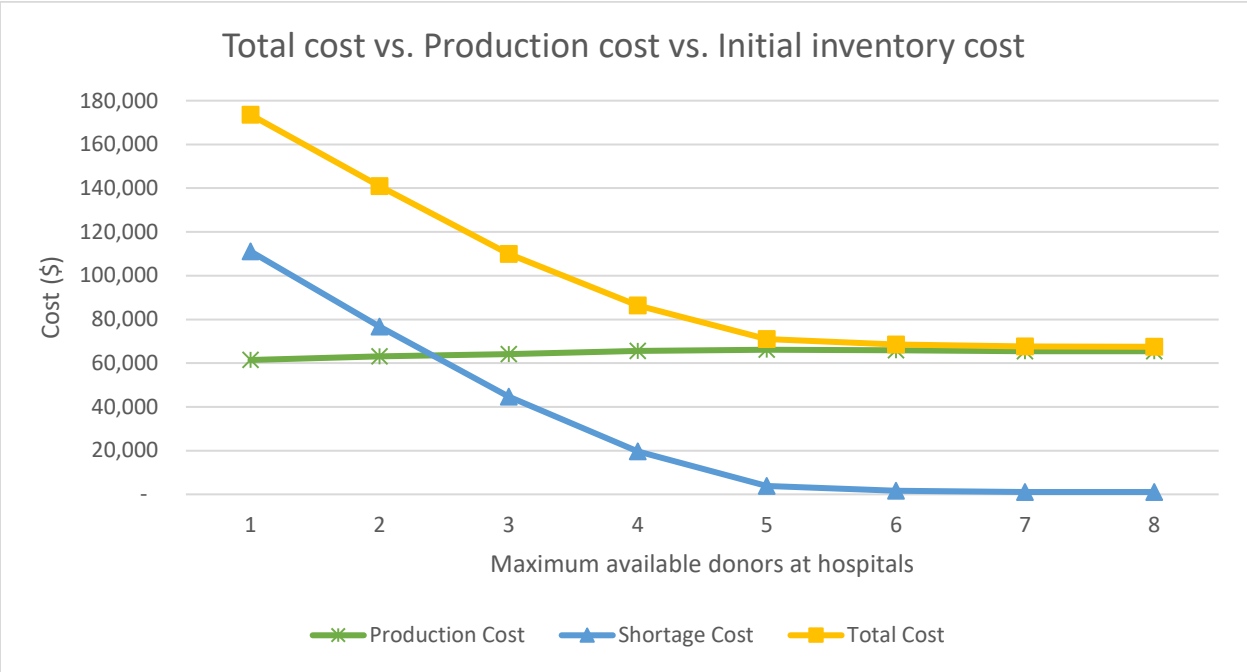


**Figure 15. Result of costs with different maximum available donors at hospitals**

Now we evaluate the impact of transshipment on system performance by comparing the existing model with a model that doesn't consider transshipment between hospitals. Total cost, inventory holding cost, production cost, transportation cost, and shortage cost are performance measurements. Table 22 shows the average percentage change of these costs for a model without transshipment compared to the model with transshipment under different maximum number of available donors at each hospital. First, we check the base case when the maximum number of available donors is 5, the total cost increases by 6.82% without transshipment. This is due to the 123% increase in shortage cost. Transportation cost also increases substantially for the model without transshipment. These results indicate that transshipment helps with improving the performance of the platelet supply chain by alleviating shortage and reallocating inventory stock

at hospitals. Next, we compare the impacts of transshipment under different maximum number of available donors at hospitals. As we can see in Table 22, transshipment works best when the number of donors is 5, while transshipment doesn't have much impact on performance improvement when the number of donors is below 3 or above 7. We can conclude that the function of transshipment is negligible for a platelet supply chain with too few or too many donors. Due to the fact that daily registered donors can satisfy around half of daily demand of blood products (ABC News, 2013), transshipment is a good strategy to alleviate shortage in supply.

**Table 22. Effect of maximum donors on change in costs for no transshipment compared to transshipment**

| Maximum # of Donors | Total cost | Holding cost | Production cost | Transportation cost | Shortage cost |
|---|---|---|---|---|---|
| **1** | 0.03% | 0.00% | 0.00% | 80.78% | 0.00% |
| **2** | 0.16% | 0.07% | 0.05% | 90.42% | 0.16% |
| **3** | 2.24% | 0.65% | 0.11% | 101.94% | 5.21% |
| **4** | 3.26% | 0.49% | -0.05% | 115.84% | 14.16% |
| **5** | 6.82% | -0.03% | 0.16% | 146.92% | 122.84% |
| **6** | 2.49% | 0.47% | 0.34% | 166.03% | 86.64% |
| **7** | 1.07% | 0.24% | 0.25% | 197.86% | 46.09% |
| **8** | 0.50% | -0.01% | 0.30% | 203.60% | 7.54% |

#### *3.5.4.2. Impact of capacity level on total cost*

Figure 16 shows the impact of different capacity levels at the blood center on total cost. Our base case considers a capacity level of 90 units at the blood center. When the capacity at the blood center increases from 30 to 60 units, total cost decreases dramatically for the platelet supply chain. When the capacity increases from 70 to 100 units, total cost shows a decreasing trend at a smaller rate. When capacity is over 100 units, total cost no longer decreases. The blood center capacity has a positive effect on supply chain performance within a certain range. In our

example, to achieve the optimal performance, the blood center should manage a capacity of 100 units.

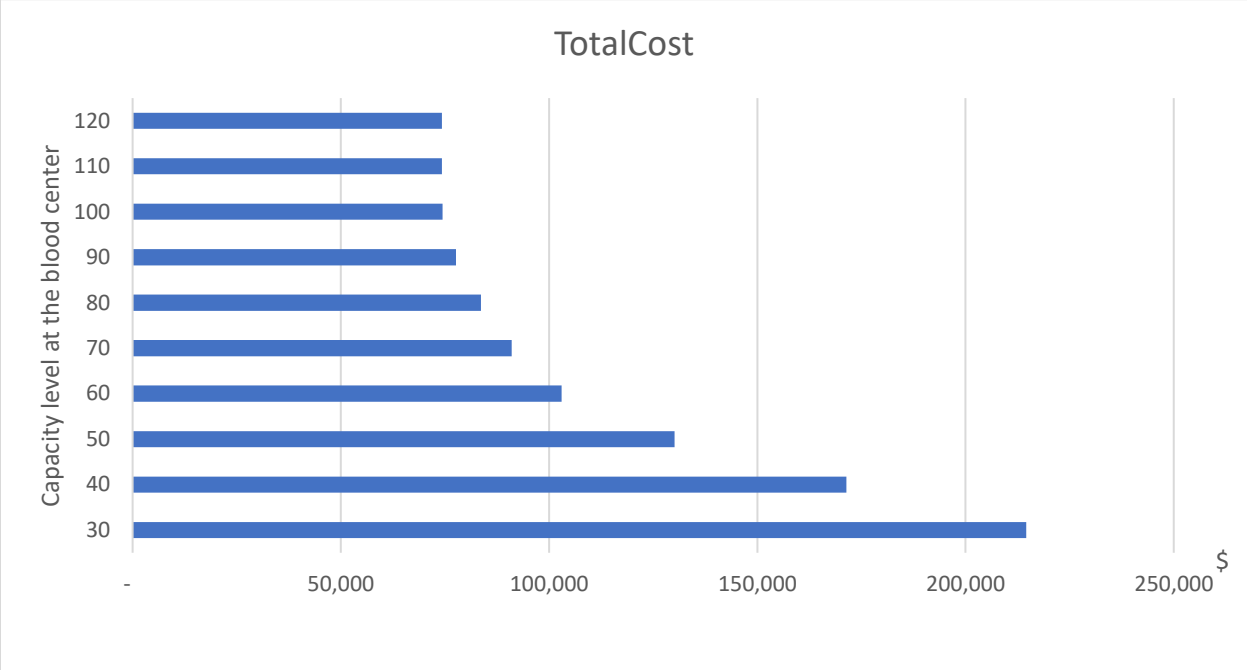


**Figure 16. Total cost for different capacity levels at the blood center**

Now we assess the effects of transshipment on system performance by comparing the existing model with a model that doesn't consider transshipment under different capacity levels for the blood center. Total cost, inventory holding cost, production cost, transportation cost, and shortage cost are still used as performance measurements. Table 23 shows the percentage change of these costs for a model without transshipment compared to the existing model under diverse capacity levels. For the base case when the capacity is 90 units, the total cost increases by 8% without transshipment. Transshipment works best when the capacity at the blood center is 30, as the total operational cost will increase by 22% without transshipment. When the capacity is 110 or above, the improvements of transshipment on system performance are exactly the same. We can conclude that transshipment benefits platelet supply chain with limited blood center capacity.

It is likely more cost effective to implement transshipment between hospitals than increasing capacity of blood centers for improving performance of platelet supply chains.

**Table 23. Effect of capacity on change in costs for no transshipment compared to transshipment**

| Capacity | Total cost | Holding cost | Production cost | Transportation cost | Shortage cost |
|---|---|---|---|---|---|
| **30** | 22% | -4% | -5% | 84% | 31% |
| **40** | 13% | 0% | -1% | 121% | 21% |
| **50** | 12% | -2% | -2% | 144% | 24% |
| **60** | 15% | -2% | -2% | 146% | 43% |
| **70** | 15% | -2% | -1% | 143% | 59% |
| **80** | 10% | -3% | -1% | 142% | 59% |
| **90** | 8% | -5% | -2% | 131% | 87% |
| **100** | 5% | -3% | -1% | 123% | 104% |
| **110** | 1% | -1% | 1% | 132% | 5% |
| **120** | 1% | -1% | 1% | 133% | 3% |

### 3.5.5. Comparison with a perfect information model

Finally, the proposed model is compared with a deterministic model to measure the differences between the proposed model and a perfect information model. As demand is known when making production plans at the blood center and placing orders at hospitals, the deterministic model is considered perfect. Total cost, inventory holding cost, production cost, transportation cost, and initial inventory cost are performance measurements. The same 15 groups of demand data generated in section 4.3 are used to conduct experiments. For the deterministic model, all 480 (15*32) combinations are solved to get average costs.

Comparisons of average costs for stochastic and deterministic models are shown in Table 24. The total cost is about $75,938 for the deterministic model, and $78,407 for the stochastic model. The total cost only increased by 3.25% for the proposed stochastic model. The increase in total cost mainly comes from increased production cost and shortage cost for the stochastic

model. Production cost and shortage cost are increased by 3.22% and 3.06%, respectively. Further, inventory holding cost and transportation cost for the stochastic model are both larger than that of the deterministic model. Considering the relatively small percentage increase on total cost, we can conclude that the proposed stochastic model is useful at dealing with random demand for an integrated platelet supply chain.

**Table 24. Comparisons of different costs for stochastic and deterministic models**

| | Deterministic model | Stochastic model | Change |
|---|---|---|---|
| **Production cost** | 65,104.95 | 67,201.07 | 3.22% |
| **Holding cost** | 872.94 | 942.43 | 7.96% |
| **Shortage cost** | 9,812.50 | 10,112.50 | 3.06% |
| **Transportation cost** | 83.33 | 87.81 | 5.37% |
| **Transshipment cost** | 63.86 | 63.28 | -0.91% |
| **Total cost** | 75,937.58 | 78,407.09 | 3.25% |

## 3.6. Conclusion

We formulated a multi-stage stochastic program of an integrated platelet supply chain that aims to provide tactical and operational decisions on the quantity of blood and platelets collected, the quantity of platelets produced at the blood center, the quantity of platelets delivered to hospitals, and the quantity of transshipment between hospitals under different demand scenarios. The application of the proposed model was demonstrated with a real-world platelet supply chain which consists of one blood center, three collection facilities, and five hospitals in the Fargo-Moorhead area, which is located in North Dakota and Minnesota, USA. The objective was to minimize total operational cost including production, transportation, inventory, transshipment, shortage and outdating costs. Our numerical results indicate that the proposed model is good at dealing with random demand and transshipment does help with alleviating shortage and reallocating stock at hospitals and improving system cost efficiency,

especially when capacity at the blood center is limited. We also conclude that recruiting more apheresis platelet donors at hospitals is an alternative strategy to improve performance of platelet supply chains. In contrast, increasing capacity at blood centers can reduce costs, to a point, but is not a substitute for transshipments.

There are several research directions that can be pursued at this point. First, considering multiple blood products such as red blood cells and platelets within the blood supply chain network. As donated whole blood can be separated into red blood cells, platelets and plasma, considering multiple products is necessary for accurate modeling of supply and demand. Second, developing a larger supply chain where more blood centers and hospitals are involved. Large cities such as Chicago normally have several blood centers that cooperate and compete with each other. Third, the consideration of combining proactive with reactive transshipments in a shorter time frame to examine intraday reactions in the platelet supply chain. This is extremely important during a blood shortage crisis.

# CHAPTER 4. A MULTI-PRODUCT MULTI-PERIOD STOCHASTIC MODEL FOR A BLOOD SUPPLY CHAIN CONSIDERING BLOOD SUBSTITUTION AND DEMAND UNCERTAINTY

## 4.1. Abstract

This paper presents a multi-product multi-period stochastic program for an integrated blood supply chain that considers red blood cells and platelets while accounting for multi-product interactions, demand uncertainty, blood age information, blood type substitution, and three types of patients. The aim is to minimize the total cost incurred during the collection, production, inventory, and distribution echelons under centralized control. The supply chains for red blood cells and platelets intertwine at the collection and production echelons as collected whole blood can be separated into red blood cells and platelets at the same time. By adapting to a real-world blood supply chain with one blood center, three collection facilities, and five hospitals, we found the cost advantage of the multi-product model over an uncoordinated model where the red blood cell and platelet supply chains are considered separately. Further sensitivity analyses indicated that cost savings of the multi-product model mainly come from variations in the number of apheresis donors. An increase in whole blood donors can hurt the performance of the supply chain if a multi-product model is not used.

## 4.2. Introduction

Blood is an unmanufacturable and irreplaceable product that is necessary for surgeries and treatment of patients suffering from illnesses and accidents. There are more than 4,000 different kinds of components contained in blood. Of all these blood components, the three most important are red blood cells (RBC), platelets (PLT), and plasma (PLS). According to American Red Cross (2016), daily demands for red blood cells, platelets, and plasma are approximately

36,000, 7,000, and 10,000 units respectively in the United States. Red blood cells are the most abundant cell type and can be stored for up to 42 days after collection (American Red Cross, 2017a). Although demand of platelets only accounts for around 1/5 of red blood cells, they play an important role in organ transplants, bone marrow transplants, cancer treatment and general surgeries. Platelets are the most perishable blood product and have a shelf life of 5 days (American Red Cross, 2017a). Unlike red blood cells and platelets, plasma is not a perishable product and can be stored for nearly 1 year (American Red Cross, 2017a). Handling supply chain management of plasma is significantly less complex than platelets and red blood cells with regard to balancing wastage and shortage. Therefore, this research focuses on optimizing the supply chain management of red blood cells and platelets.

Generally, the blood supply chain is divided into four echelons: collection, production, inventory, and distribution. There are several similarities and differences between the RBC and PLT supply chains for each echelon. Both supply chains start with blood collection from donors. There are two ways of collecting red blood cells or platelets: through whole blood or apheresis. Whole blood donation is the most common donation type and it usually takes about 10 to 20 minutes. One unit of whole blood can be mechanically processed to produce one unit of red blood cells and one unit of platelets. The apheresis process takes longer than that of whole blood donation, approximately one to two hours. One apheresis donation can contribute two units of red blood cells or four to six units of platelets (American Red Cross, 2017b). Whole blood and apheresis derived red blood cells are collected by bloodmobiles. Whole blood is then separated into red blood cells, platelets, and plasma. Platelets and red blood cells are collected by apheresis at blood centers and hospitals. Collected whole blood, red blood cells, and platelets are tested for different infectious diseases. Once appropriate for use, red blood cells and platelets are allocated

to inventories at blood centers or hospitals. Red blood cells need to be stored in refrigerators at a temperature between 2 to 6℃. In contrast, platelets can be kept at room temperature but need to be agitated constantly to avoid clumping. These blood products are then distributed from blood centers to hospitals to satisfy transfusion demand from patients.

For red blood cells, it is necessary to consider crossmatching of blood types between donors and patients before transfusion as not all blood types are compatible. There are eight main blood types: A, B, AB and O, each of which can be rhesus positive or negative. Table 25 shows the compatibility chart for substitution of blood types for red blood cells (Dillon et al. 2017). As illustrated in Table 25, a person with blood type AB+ is a universal recipient who can receive blood from donors with any blood type. In an analogous fashion, a person with blood type O- is known as a universal donor. But for platelets, while transfusing the same ABO type as the patient is the first choice, any ABO and rhesus type is possible. However, platelet demand can be classified into three types based on patients' needs as shown in Table 26 (Ensafian & Yaghoubi, 2017). Fresh, young, and old platelets are defined as platelets with an age of one day old, two to three days old, and four to five days, respectively. Fresh platelets are needed for organ or bone marrow transplantation. Fresh or young platelets are needed for oncology and hematology cases or cancer treatment. Other patients can use fresh, young, or old platelets.

Most literature regarding blood supply chain management considers a single blood product such as red blood cells or platelets, we are unaware of any study that discusses a multi-product blood supply chain which takes stock age information into account. According to Barbee (2013), in 2011 donation of whole blood was approximately 13,744,000 units, in addition, nearly 1,978,000 units of red blood cells and 2,516,000 units of platelets were collected by apheresis. As an important source of blood supply, whole blood donation has great effects on both the red

blood cell and platelet supply chains. Therefore, it is necessary to consider multiple products for accurate modeling of supply of the blood supply chain.

**Table 25. Compatibility chart for red blood cells**

| | Donor blood type | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Patient blood type | A+ | A- | B+ | B- | AB+ | AB- | O+ | O- |
| A+ | Y | Y | - | - | - | - | Y | Y |
| A- | - | Y | - | - | - | - | - | Y |
| B+ | - | - | Y | Y | - | - | Y | Y |
| B- | - | - | - | Y | - | - | - | Y |
| AB+ | Y | Y | Y | Y | Y | Y | Y | Y |
| AB- | - | Y | - | Y | - | Y | - | Y |
| O+ | - | - | - | - | - | - | Y | Y |
| O- | - | - | - | - | - | - | - | Y |

**Table 26. Demand type for platelets**

| **Demand type** | **Age** | **Usage** |
|---|---|---|
| Fresh | 1 day old | Organ transplantation and bone marrow |
| Young | 2-3 days old | Hematology, oncology, and cancer treatment |
| Old | 4-5 days old | Traumatology and general surgery |

This paper presents a novel multi-product multi-period stochastic program for a four-echelon blood supply chain that considers red blood cells and platelets while accounting for blood type substitution and three types of patients. The impacts of performing blood type substitution of red blood cells are evaluated by adding a penalty cost. In addition, to deal with large demand differences between red blood cells and platelets when they are sharing part of a blood supply, we allow excess platelets produced to be shipped out of the system and absorbed by the global blood supply chain. Similarly, an out shipping cost is taken into account for platelet units shipped out of the system. The objective of the proposed model is to minimize total costs, including production, transportation, inventory, shortage, outdate, penalty, and out shipping costs, under a centralized control system where any decision regarding production and allocation

is made with a system-wide perspective. By adapting our model to a real-world case study from the Fargo-Moorhead area, North Dakota and Minnesota, USA, we found the cost advantage of a multi-product blood supply chain over an uncoordinated model where the red blood cell and platelet supply chains are considered separately. Further sensitivity analyses on exploring the impacts of whole blood donors and apheresis donors for red blood cells on system performance indicated that cost savings of the multi-product model mainly come from variations in the number of apheresis donors. An increase in whole blood donors can actually hurt the performance of the supply chain if a multi-product model is not used to coordinate production of red blood cells and platelets.

### 4.3. Literature review

Literature regarding the blood supply chain has been extensively explored in recent years. However, there still exist research gaps for some areas. Beliën and Forcé (2012) identified five dominant significant blood products through their review of applications on the blood supply chain, which are whole blood, red blood cells, platelets, plasma, and frozen blood. Plasma and frozen blood are less explored compared to other blood products as they are nonperishable. Whole blood is now seldomly used as a transfusable product, but it is an important blood donation type and is thus commonly considered when the research deals with donor issues. Red blood cells and platelets are the main research focuses. However, although there is a vast of literature focusing on the supply chain management of red blood cells or platelets, very few studies consider these two blood products at the same time. In this section, we present the relevant literature on the RBC and PLT supply chains respectively, as well as the multi-product supply chain.

Red blood cells are the mostly demanded blood components. A considerable amount of research has been dedicated to RBC supply chain. One important characteristic that needs to be considered is blood type substitution. Models that do not consider different ABO blood types for red blood cells, such as in Fahimnia et al. (2017), Wang and Ma (2015), and Gunpinar and Centeno (2015) might be infeasible as not all blood collected is suitable to be transfused to patients with a certain blood type. Most recent works consider blood type compatibility and substitution when formulating models for red blood cells (Hamdan & Diabat, 2019; Najafi et al., 2017; Dillon et al., 2017; Duan & Liao, 2014). Dillon et al. (2017) introduced a two-stage stochastic program for red blood cell inventory management that focused on minimizing operational costs, as well as blood shortage and wastage. Najafi et al. (2017) developed a model to manage ordering and issuing policies for red blood cells in a hospital considering age information, blood type substitution, supply and demand uncertainty, and transshipment possibility. However, these two papers focused only on a single echelon which is inventory. Hamdan and Diabat (2019) presented a mathematical model for an integrated RBC supply chain that seeks to minimize total system cost, processing and transportation time, and number of outdated units. The model accounts for blood type substitution, product perishability, stochastic supply, and stochastic demand. Though this research considered perishability of red blood cells, it didn't provide age information of red blood cells in the inventory. Another limitation is that only whole blood donation was considered as a source of supply for red blood cells without considering apheresis donation.

Platelets are much more perishable compared to red blood cells as they have a very short shelf life. Blake (2009) stated that the age information of platelets in the inventory plays a very important role in optimizing the blood supply chain. Tekin et al. (2001) also indicated that an

age-based policy was superior to policies without age considerations. Thus, more and more recent studies consider age-based platelet supply chains or inventory models (Duan & Liao, 2013; Abdulwahab & Wahab, 2014; Gunpinar & Centeno, 2015; Ensafian & Yaghoubi, 2017; Ensafian et al., 2017). To the best of our knowledge, Duan and Liao (2013) were the first to develop a quantitative model of inventory management of platelets that considers age information. However, their framework was based on a simulation optimization approach which would be time-consuming to determine favorable operating conditions. Gunpinar and Centeno (2015) developed a stochastic integer program for a two-level supply chain consisting of one blood center and one hospital that explicitly accounts for the age of blood units, demand for two types of patients, and demand uncertainty. On the basis of Gunpinar and Centeno (2015), Ensafian and Yaghoubi (2017) enlarged the platelet supply chain both horizontally and vertically by considering four echelons including collection, production, inventory, and distribution with 18 collection facilities, one blood center, and 10 hospitals. They considered two collection approaches of platelets and three different types of patients. Further, Ensafian et al. (2017) developed the stochastic mixed-integer model further by applying a discrete Markov Chain Process to predict the number of donors and incorporating ABO-Rh priority matching rules for platelets.

Although research regarding multi-product supply chains for nonperishable items is common (Altiparmak et al., 2009; Liang, 2008; Mirzapour et al., 2011; Paksoy et al., 2011), there is little work that addresses perishable products. Shaabani and Kamalabadi (2016) presented a mathematical model for a multi-product multi-retailer inventory routing problem where perishable products were involved. To achieve the objective of minimizing total cost while ensuring no stock outs, a population-based simulated annealing algorithm was proposed.

The first study that considered multiple perishable products was Deuermeyer and Pierskalla (1978). They considered a new system with two products and two production processes where one of the production processes was capable to produce both products. This is exactly what we saw in the blood supply chain in which whole blood donation can generate both red blood cells and platelets while apheresis donation can generate either red blood cells or platelets. Arvan et al. (2015) presented an integrated supply chain that includes donation sites, testing and processing labs, blood banks and demand points. Four blood products were considered in the proposed model: whole blood, red blood cells, plasma and platelets. The goals were minimizing the total operational cost and the total time that blood products remain in the network before being consumed. However, this model didn't account for apheresis donation as well as shortages and outdates of blood products. Osorio et al. (2016) presented a combination of an integrated simulation-based model and an integer linear optimization model focusing on the collection and production echelons that accounts for blood type substitution and perishability. This study considered four blood products: red blood cells, plasma, platelets, and cryoprecipitate, and five production processes: whole blood fractionation using triplex bag, quadruple bag A, and quadruple bag B respectively, and apheresis production for red blood cells and platelets. However, the proposed optimization model was limited to the collection and production stages and the age information of products in the inventory was unknown. Zahiri and Pishvaee (2017) formulated a novel multi-period location allocation problem for a blood supply chain that focused on minimizing total costs and unmet demand. This research considered multiple blood products, which are red blood cells, platelets, and plasma. In addition, blood type substitution for red blood cells and plasma were taken into account. However, the model didn't use shortages and outdates in accounting for inventory, which limits its usefulness.

To the best of our knowledge, there are no studies that formulate an integrated blood supply chain model that considers multiple blood products and multiple production processes. As both red blood cells and platelets can be produced through whole blood and apheresis, and whole blood separation can generate both blood products, it is necessary to consider a multi-product blood supply chain so as to coordinate different types of production processes and maintain an appropriate inventory level. Therefore, the main contribution of this study is that we present the first multi-product multi-period stochastic program for integrated blood supply chain that accounts for demand uncertainty, age information, blood type substitution, and demand types for platelets.

### 4.4. Problem description

In this study, we investigate a centralized blood supply chain system with multiple perishable products within multiple periods considering one regional blood center, several blood collection facilities and hospitals. The aim is to minimize the total cost incurred in the collection, production, inventory, and distribution echelons. As a multi-product system, two supply chains are actually considered: the RBC supply chain and the PLT supply chain. The two supply chains intertwine at the collection and production echelons through whole blood donation and separation.

The structure of the blood supply chain is depicted in Figure 17. There are three types of facilities considered: bloodmobiles, the blood center, and hospitals. All of these facilities can be used for collecting blood, but bloodmobiles can only collect whole blood and apheresis derived red blood cells, and the blood center and hospitals mainly collect apheresis derived red blood cells and platelets. Blood units collected through bloodmobiles are then transported to the blood center and separated into red blood cells and platelets. Thus, inventory of whole blood is

considered to be zero. After performing bacterial testing, suitable blood products are either put into inventory or distributed to different hospitals. In addition, platelets can be shipped out of the system to fulfil demand of the global blood supply chain. Three types of patients are taken into account for platelets and blood type crossmatching and substitution is considered for red blood cells.

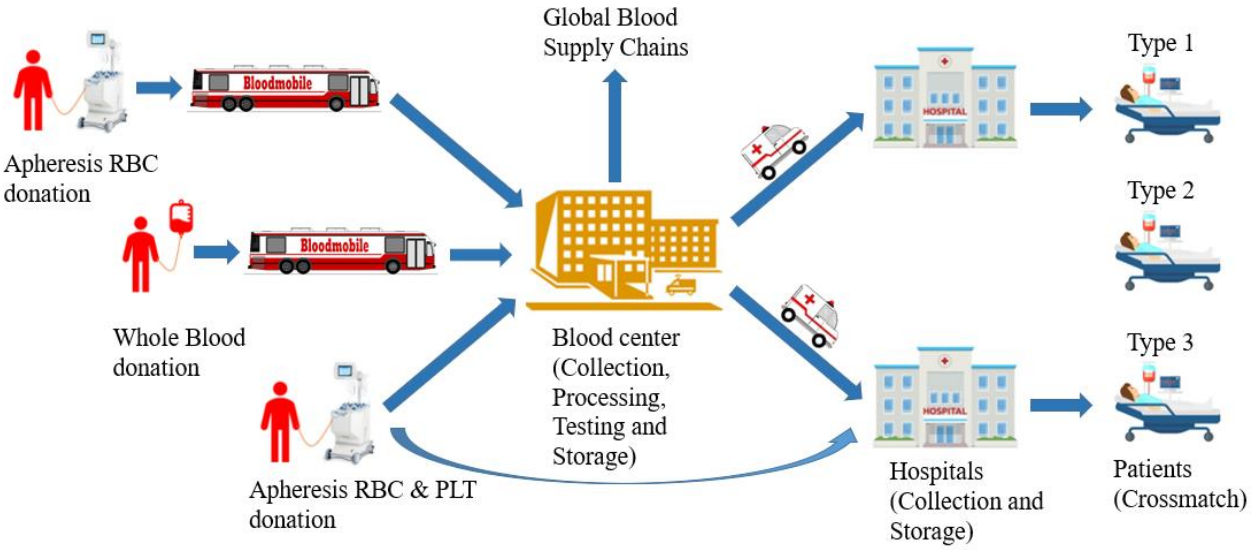


**Figure 17. Platelet supply chain network**

Within the multi-period supply chain, the demand for both blood products differs day by day, as does the production schedule at the blood center. Each hospital orders each blood product based on estimated demand and remaining inventory before the start of each day. At the beginning of each day, the blood center distributes ordered blood products to different hospitals, then updates its current inventory by adding newly collected or produced units and removing any expired units as well as units that have been distributed, and finally making a new production plan based on remaining inventory and estimated total orders from the hospitals. On the other hand, hospitals receive different blood products with different age distributions from the blood center. These received units together with the units stored at the inventory of each hospital are

used for satisfying different types of demand. Since demand for red blood cells and platelets fluctuates day by day and is unknown when operational decisions are made, it is necessary to address the issue of demand uncertainty. According to Birge and Louveaux (2011), stochastic programming is a useful and popular approach to deal with uncertainty. Therefore, a multi-period stochastic program is applied to the blood supply chain. For each day, the supply of whole blood and apheresis derived blood products is decided prior to the realization of uncertainty, while other decisions including production, distribution, and inventory are made without knowing the specific demand for each product.

According to the above description, the main assumptions of the blood supply chain are listed as follows:

- It takes two days to process and test whole blood units (Ensafian & Yaghoubi, 2017), while only one day is needed for performing bacterial tests on apheresis derived blood products according to a manager from a local blood center.
- Demand for red blood cells is much larger than demand for platelets (American Red Cross, 2016). Therefore, to satisfy demand for red blood cells, a large amount of whole blood units will be collected as an important source of supply. This may mean excess platelets that are separated from whole blood can't be absorbed by the current supply chain system and have to be distributed to other blood supply chains. This practice was testified to by a manger from a local blood center.
- Lead time for transportation between any two facilities is zero and doesn't have any influence on the age of transported blood units. As we are considering a blood supply chain in a local area, geographic distance between the collection sites and the blood center or between the blood center and hospitals is relatively small.

## 4.5. Mathematical formulation

### 4.5.1. Model notation

The complete notation for the multi-product supply chain model is summarized as follows.

**Table 27. Notation used in the multi-product blood supply chain model**

| **Sets** | **Description** |
|---|---|
| $N$ | Age of blood products, $n \in N$ |
| $K$ | Demand type for blood products, $k \in K$ |
| $I$ | Hospitals, $i \in I$ |
| $J$ | Blood collection facilities, $j \in J$ |
| $T$ | Time periods, $t \in T$ |
| $E$ | Blood types, $\alpha, \alpha' \in E$ |
| $\Gamma$ | Different blood product types, $\sigma \in \Gamma$ |
| $\Xi$ | Scenarios, $\varepsilon \in \Xi$ |
| | |
| **Parameters** | |
| $\gamma$ | Fraction of valid whole blood units used for separation process |
| $\beta_\sigma$ | Quantity of blood product type σ obtained from one apheresis donation |
| $N_\sigma$ | Lifetime of blood product σ |
| $W_{jt\alpha}$ | Number of whole blood donors with blood type $\alpha$ at collection facility $j$ on day $t$ |
| $X_{jt\alpha\sigma}$ | Number of apheresis donors with blood type $\alpha$ for blood product σ at collection facility $j$ on day $t$, $\sigma =$ RBC |
| $X_{it\alpha\sigma}$ | Number of apheresis donors with blood type $\alpha$ for blood product σ at hospital $i$ on day $t$ |
| $X_{0t\alpha\sigma}$ | Number of apheresis donors with blood type $\alpha$ for blood product σ at the blood center on day $t$ |
| $F$ | Fixed cost of producing blood components from whole blood at the blood center |
| $V$ | Operation cost per unit of whole blood separation at the blood center |
| $p_\sigma$ | Apheresis production cost per unit of blood product σ |
| $h_\sigma$ | Unit holding cost of blood product σ per day |
| $G_j$ | Unit transportation cost from blood collection facility $j$ to the blood center |
| $H_i$ | Unit transportation cost from the blood center to hospital $i$ |
| $w$ | Unit transportation cost of platelets shipped out of system |
| $u_\sigma$ | Shortage cost per unit of blood product σ |
| $v_\sigma$ | Outdating cost per unit of blood product σ |
| $g_{\alpha\alpha'}$ | Penalty cost for substituting blood type $\alpha$ with type $\alpha'$ |
| $d_{itk\alpha\sigma\varepsilon}$ | Patient demand of type $k$ and blood type $\alpha$ for blood product σ at hospital $i$ on day $t$ under scenario $\varepsilon$ |
| $D_{k\sigma}$ | Set of ages for blood product σ associated with demand type $k$ |

**Table 27. Notation used in the multi-product blood supply chain model (continued)**

| Parameters | Description |
|---|---|
| $\pi_{\alpha\alpha'}$ | 1 if the demand for blood type $\alpha$ can be alternatively fulfilled with blood type $\alpha'$, 0 otherwise |
| $C_{i\sigma}$ | Capacity of blood product σ at hospital $i$ |
| $C_{0\sigma}$ | Capacity of blood product σ at the blood center |
| $P_{\varepsilon}$ | Probability of scenario $\varepsilon$ |
| **Variables** | |
| $A_{it\alpha\sigma}$ | Quantity of apheresis donation for blood product σ with blood type $\alpha$ at hospital $i$ on day $t$ |
| $A_{0t\alpha\sigma}$ | Quantity of apheresis donation for blood product σ with blood type $\alpha$ at the blood center on day $t$ |
| $A_{jt\alpha\sigma}$ | Quantity of apheresis donation for blood product σ with blood type $\alpha$ at collection facility $j$ on day $t$, $\sigma = \mathrm{RBC}$ |
| $B_{jt\alpha}$ | Quantity of whole blood donation with blood type $\alpha$ at collection facility $j$ on day $t$ |
| $Q_{t\alpha\sigma}$ | Quantity of blood product σ with blood type $\alpha$ produced from whole blood at the blood center on day $t$ |
| $I_{itn\alpha\sigma\varepsilon}$ | Quantity of blood product σ aged $n$ with blood type $\alpha$ in the inventory of hospital $i$ at the beginning of day $t$ under scenario $\varepsilon$ |
| $I_{0tn\alpha\sigma\varepsilon}$ | Quantity of blood product σ aged $n$ with blood type $\alpha$ in the inventory of the blood center at the beginning of day $t$ under scenario $\varepsilon$ |
| $R_{itn\alpha\sigma\varepsilon}$ | Quantity of blood product σ aged $n$ with blood type $\alpha$ shipped to hospital $i$ on day $t$ under scenario $\varepsilon$ |
| $Y_{tn\alpha\sigma\varepsilon}$ | Quantity of blood product σ aged $n$ with blood type $\alpha$ shipped out of system on day $t$ under scenario $\varepsilon$, $\sigma = \mathrm{PLT}$ |
| $S_{itk\alpha\sigma\varepsilon}$ | Shortage quantity of blood product σ for demand type $k$ and blood type $\alpha$ at hospital $i$ on day $t$ under scenario $\varepsilon$ |
| $O_{it\sigma\varepsilon}$ | Outdated quantity of blood product σ at hospital $i$ on day $t$ under scenario $\varepsilon$ |
| $O_{0t\sigma\varepsilon}$ | Outdated quantity of blood product σ at the blood center on day $t$ under scenario $\varepsilon$ |
| $U_{itn\alpha\alpha'\sigma\varepsilon}$ | Quantity of blood product σ aged $n$ with blood type $\alpha'$ in the inventory of hospital $i$ used to satisfy demand of blood type $\alpha$ on day $t$ under scenario $\varepsilon$, $\forall\, i,t,n,\sigma,\pi_{\alpha\alpha'} = 1$ |
| $Z_t$ | 1 if blood products are produced from whole blood at the blood center on day $t$, 0 otherwise |

### 4.5.2. Mathematical model

Base on the defined parameters and variables, a multi-stage multi-product stochastic model is formulated as follows.

$$Min\ \sum_{t=1}^{T} F * Z_t + \sum_{\sigma}\sum_{\alpha}\sum_{t=1}^{T} V * Q_{t\alpha\sigma}/2 + \sum_{\sigma}\sum_{\alpha}\sum_{t=1}^{T} p_\sigma * A_{0t\alpha\sigma} +$$
$$\sum_{\sigma}\sum_{\alpha}\sum_{t=1}^{T}\sum_{i=1}^{I} p_\sigma * A_{it\alpha\sigma} + \sum_{\sigma}\sum_{\alpha}\sum_{t=1}^{T}\sum_{j=1}^{J} p_\sigma * A_{jt\alpha\sigma} + \sum_{\alpha}\sum_{t=1}^{T}\sum_{j=1}^{J} G_j *$$
$$(B_{jt\alpha} + \sum_{\sigma} A_{jt\alpha\sigma}) + \sum_{\varepsilon}\sum_{\sigma}\sum_{\alpha}\sum_{t=1}^{T}\sum_{i=1}^{I}\sum_{n=1}^{N_\sigma} P_\varepsilon * H_i * R_{itn\alpha\sigma\varepsilon} +$$
$$\sum_{\varepsilon}\sum_{\sigma}\sum_{\alpha}\sum_{t=1}^{T}\sum_{i=1}^{I}\sum_{n=1}^{N_\sigma} P_\varepsilon * h_\sigma * I_{itn\alpha\sigma\varepsilon} + \sum_{\varepsilon}\sum_{\sigma}\sum_{\alpha}\sum_{t=1}^{T}\sum_{n=1}^{N_\sigma} P_\varepsilon * h_\sigma * I_{0tn\alpha\sigma\varepsilon} +$$
$$\sum_{\varepsilon}\sum_{\sigma}\sum_{\alpha}\sum_{k=1}^{K}\sum_{t=1}^{T}\sum_{i=1}^{I} P_\varepsilon * u_\sigma * S_{itk\alpha\sigma\varepsilon} + \sum_{\varepsilon}\sum_{\sigma}\sum_{t=1}^{T}\sum_{i=1}^{I} P_\varepsilon * v_\sigma * O_{it\sigma\varepsilon} +$$
$$\sum_{\varepsilon}\sum_{\sigma}\sum_{t=1}^{T} P_\varepsilon * v_\sigma * O_{0t\sigma\varepsilon} + \sum_{\varepsilon}\sum_{\sigma}\sum_{\alpha}\sum_{n=2}^{N} P_\varepsilon * (I_{01n\alpha\sigma\varepsilon} + \sum_{i=1}^{I} I_{i1n\alpha\sigma\varepsilon}) * (V +$$
$$h_\sigma) + \sum_{\varepsilon}\sum_{\sigma=RBC}\sum_{\alpha}\sum_{\alpha'}\sum_{t=1}^{T}\sum_{i=1}^{I}\sum_{n=1}^{N_\sigma} P_\varepsilon * g_{\alpha'\alpha} * U_{itn\alpha'\alpha\sigma\varepsilon} +$$
$$\sum_{\varepsilon}\sum_{\sigma=PLT}\sum_{\alpha}\sum_{t=1}^{T}\sum_{n=1}^{N_\sigma} P_\varepsilon * w * Y_{tn\alpha\sigma\varepsilon} \qquad (4.1)$$

s.t.

$$\sum_{\alpha} Q_{t\alpha\sigma} \le C_{0\sigma} * Z_t \qquad \forall t, \sigma \qquad (4.2)$$

$$\sum_{\alpha}\sum_{n=1}^{N_\sigma - 1} I_{0tn\alpha\sigma\varepsilon} \le C_{0\sigma} \qquad \forall t, \sigma, \varepsilon \qquad (4.3)$$

$$\sum_{\alpha}\sum_{n=1}^{N_\sigma - 1} I_{itn\alpha\sigma\varepsilon} \le C_{i\sigma} \qquad \forall i, t, \sigma, \varepsilon \qquad (4.4)$$

$$B_{jt\alpha} \le W_{jt\alpha} \qquad \forall j, t, \alpha \qquad (4.5)$$

$$A_{it\alpha\sigma} \le X_{it\alpha\sigma} \qquad \forall i, t, \alpha, \sigma \qquad (4.6)$$

$$A_{0t\alpha\sigma} \le X_{0t\alpha\sigma} \qquad \forall t, \alpha, \sigma \qquad (4.7)$$

$$A_{jt\alpha\sigma} \le X_{jt\alpha\sigma} \qquad \forall j, t, \alpha, \sigma = RBC \qquad (4.8)$$

$$Q_{(t+2)\alpha\sigma} \le \sum_{j=1}^{J} B_{jt\alpha} * \gamma \qquad \forall \alpha, \sigma, t = 1, \dots, T-2 \qquad (4.9)$$

$$I_{0(t+1)n\alpha\sigma\varepsilon} = I_{0t(n-1)\alpha\sigma\varepsilon} - \sum_{i=1}^{I} R_{it(n-1)\alpha\sigma\varepsilon} - Y_{t(n-1)\alpha\sigma\varepsilon}$$
$$\forall \varepsilon, \alpha, \sigma, t = 1, \dots, T-1, n = 4, \dots, N_\sigma \qquad (4.10)$$

$$I_{0(t+1)3\alpha\sigma\varepsilon} = I_{0t2\alpha\sigma\varepsilon} + Q_{(t+1)\alpha\sigma} - \sum_{i=1}^{I} R_{it2\alpha\sigma\varepsilon} - Y_{t2\alpha\sigma\varepsilon}$$
$$\forall \varepsilon, \alpha, \sigma, t = 1, \dots, T-1 \qquad (4.11)$$

$$I_{0t2\alpha\sigma\varepsilon} \ge \sum_{i=1}^{I} R_{it2\alpha\sigma\varepsilon} + Y_{t2\alpha\sigma\varepsilon} \qquad \forall \varepsilon, \alpha, \sigma, t \qquad (4.12)$$

$$I_{0(t+1)2\alpha\sigma\varepsilon} = \beta_\sigma \cdot A_{0t\alpha\sigma} + \sum_{j=1}^{J} A_{jt\alpha\sigma} \cdot \beta_\sigma \qquad \forall \varepsilon, \alpha, \sigma, t = 1, \dots, T-1 \tag{4.13}$$

$$I_{i(t+1)2\alpha\sigma\varepsilon} = \beta_\sigma \cdot A_{it\alpha\sigma} \qquad \forall \varepsilon, i, \alpha, \sigma, t = 1, \dots, T-1 \tag{4.14}$$

$$I_{i(t+1)n\alpha\sigma\varepsilon} = I_{it(n-1)\alpha\sigma\varepsilon} + R_{it(n-1)\alpha\sigma\varepsilon} - \sum_{\alpha'} U_{it(n-1)\alpha'\alpha\sigma\varepsilon}$$
$$\forall \varepsilon, i, \alpha, \alpha', \sigma, t = 1, \dots, T-1, n = 3, \dots, N_\sigma \tag{4.15}$$

$$\sum_{\alpha'} \sum_{n \in D_k} U_{itn\alpha'\alpha\sigma\varepsilon} + \sum_k S_{itk\alpha\sigma\varepsilon} \geq \sum_k d_{itk\alpha\sigma\varepsilon} \qquad \forall \varepsilon, i, t, \alpha, \sigma \tag{4.16}$$

$$\sum_\alpha I_{itn\alpha\sigma\varepsilon} = O_{it\sigma\varepsilon} \qquad \forall \varepsilon, i, t, \sigma, n = N_\sigma \tag{4.17}$$

$$\sum_\alpha I_{0tn\alpha\sigma\varepsilon} = O_{0t\sigma\varepsilon} \qquad \forall \varepsilon, i, t, \sigma, n = N_\sigma \tag{4.18}$$

$$Q_2 = 0 \tag{4.19}$$

$$\sum_{n=1}^{N-1} I_{01n\varepsilon} \leq \sum_{i=1}^{I} C_i^{Initial} \qquad \forall \varepsilon \tag{4.20}$$

$$\sum_{n=1}^{N-1} I_{i1n\varepsilon} \leq C_i^{Initial} \qquad \forall i, \varepsilon \tag{4.21}$$

$$B_{jt\alpha}, Q_{t\alpha\sigma}, A_{it\alpha\sigma}, A_{0t\alpha\sigma}, A_{jt\alpha\sigma}, O_{it\sigma\varepsilon}, O_{0t\sigma\varepsilon}, I_{itn\alpha\sigma\varepsilon}, I_{0tn\alpha\sigma\varepsilon}, Y_{tn\alpha\sigma\varepsilon}, S_{itk\alpha\sigma\varepsilon}, R_{itn\alpha\sigma\varepsilon},$$
$$U_{itn\alpha\alpha'\sigma\varepsilon} \geq 0 \tag{4.22}$$

$$Z_t \in \{0,1\} \tag{4.23}$$

The objective function (4.1) aims to minimize the expected total operational cost of the multi-product blood supply chain across all scenarios. This cost comprises of fixed and variable production costs of blood products derived from whole blood, apheresis production cost at different sites, transportation cost from collection facilities to the blood center and from the blood center to hospitals, inventory holding cost, shortage cost, outdate cost, initial inventory cost, penalty cost for blood type substitution and out shipping cost for blood units that are shipped out of the system. The cost for initial inventory is estimated to be production cost adds one-day holding cost. Penalty cost for blood type substitution only applies to red blood cells and out shipping cost only applies to platelets.

Constraint (4.2) ensures that the number of blood products derived from whole blood do not exceed capacity of the blood center. Constraints (4.3) and (4.4) are storage capacity constraints of the blood center and hospitals respectively. Constraint (4.5) guarantees that the number of whole blood donation do not exceed the available whole blood donors of each blood type at collection facilities on each day. Constraints (4.6) - (4.8) put upper limits on the number of apheresis donors for each blood product at hospitals, the blood center, and blood collection facilities, respectively. Constraint (4.9) determines the number of blood products produced from whole blood for each blood type on each day considering two days needed for collected whole blood to undergo infectious disease testing and component separation. Constraints (4.10) – (4.13) are balance constraints that update the inventory status of blood products at the blood center for each age group and blood type at the start of each day under each scenario. Constraint (4.10) states that the inventory level of blood products more than four days old equals the inventory level of the previous day minus the number of blood units transported to hospitals and shipped out of the system on the previous day. Note that only platelets will be shipped out of the system to fulfill demand in other areas. Constraint (4.11) updates the inventory status of three-day-old blood products. Blood products derived from whole blood are assigned to the three-day-old inventory on each day considering two days are required for processing and testing. Constraint (4.12) enforces that the number of blood products shipped out of the blood center cannot exceed the current inventory level at the blood center on each day under all scenarios. Constraint (4.13) shows that the inventory level of two-day-old blood products equals the quantity of blood products produced by apheresis on the previous day at the blood center and blood collection facilities. Apheresis derived blood products are assigned to the two-day-old inventory because one day is needed for testing apheresis derived blood products.

Constraints (4.14) and (4.15) are balance constraints that update the inventory status of blood products at each hospital for each age group and blood type at the start of each day under each scenario. Constraint (4.14) shows that the inventory level of two-day-old blood products equals the quantity of blood products produced by apheresis at hospitals on the previous day. Constraint (4.15) states that the inventory level of blood products more than two days old equals the previous inventory level and the quantity of blood products received from the blood center on the previous day minus the quantity of blood units used to satisfy demand on the previous day. Constraint (4.16) captures the shortage quantity of blood products for each demand type and blood type at hospitals on each day under each scenario. Note that only platelets need to consider different demand types. Fresh platelets are permitted to be transfused to patients that require fresh, young, or old platelets and young platelets are suitable to be transfused to patients that require young or old platelets. Constraints (4.17) and (4.18) capture the outdated quantity for each blood product on each day at hospitals and the blood center, respectively. Constraint (4.19) ensures that the number of blood products derived from whole blood on the second day equals zero. Constraints (4.20) and (4.21) put upper bounds for initial inventory of blood products at the blood center and hospitals, respectively. Constraints (4.22) and (4.23) define the domains of variables.

## 4.6. Computational study

### 4.6.1. Case description

In this section, a real-world multi-product blood supply chain with one blood center, three blood collection facilities, and five hospitals in the Fargo-Moorhead area is applied to test and evaluate the proposed model. This area mainly includes Fargo, North Dakota, Moorhead, Minnesota, and the surrounding communities in the United States as shown in Figure 18, in

which the geographical locations of collection sites, the blood center, and hospitals are also presented. To deal with demand uncertainty for both red blood cells and platelets, we consider five different demand scenarios with equal probability within a planning horizon of 45 days.

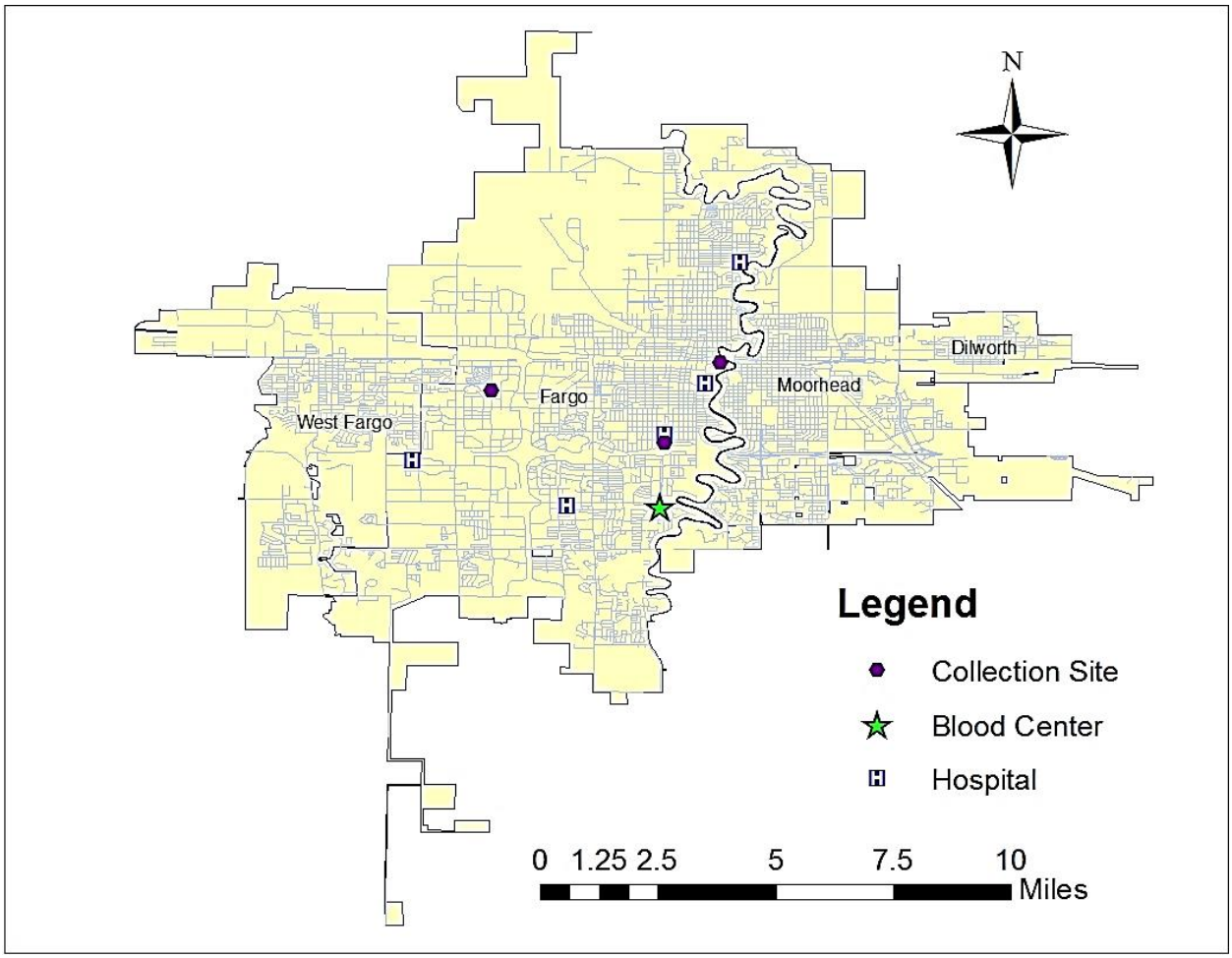


**Figure 18. The geographical locations of collection sites, the blood center, and hospitals in the Fargo-Moorhead area**

In accordance with the literature as shown in Ensafian and Yaghoubi (2017) and Haijema et al. (2007), we assume that daily demand for platelet units at each hospital follows a Poisson distribution and the mean values of daily demand at a regular hospital with around 100-150 beds are 24, 16, 32, 16, 24, 0 and 8 for Monday through Sunday respectively. For red blood cells, the mean daily demand at a regular hospital are 100, 93, 56, 59, 44, 18, and 17 for Monday through

Sunday respectively as mentioned in Gunpinar and Centeno (2015). The demand for each blood type of red blood cells is estimated to be a proportion of total demand and the proportion equals to the approximate distribution of each blood type in the US population (American Red Cross, 2019). To estimate mean daily demand of platelets and red blood cells at each considered hospital, a demand coefficient is assigned based on the number of beds at relevant hospital.

Both platelets and red blood cells can be collected from apheresis donation at the blood center and hospitals as well as whole blood donation at collection facilities. Apart from these approaches, red blood cells can also come from apheresis donation at collection sites. Table 28 presents the number of available donors for different blood products on each day in these three sites. The uniform distribution is estimated based on real data collected at different locations for available appointments under a four-month period. Not all whole blood units collected at collection facilities are suitable for producing platelets and red blood cells, thus we adopt the value of 98% for $\gamma$ to represent the percentage of appropriate whole blood in accordance with Ensafian and Yaghoubi (2017). One unit of whole blood could be separated into one unit of platelets and one unit of red blood cells, while one apheresis production can extract five units of platelets or two units of red blood cells (American Red Cross, 2017b).

**Table 28. Number of available donors**

| Type of donors | Value (unit) |
|---|---|
| Whole blood donors at collection sites | Uniform ~ [30,40] |
| Apheresis red blood cell donors at collection sites | Uniform ~ [5,10] |
| Apheresis red blood cell donors at the blood center | Uniform ~ [30,40] |
| Apheresis platelet donors at the blood center | Uniform ~ [10,15] |
| Apheresis red blood cell donors at hospitals | Uniform ~ [10,15] |
| Apheresis platelet donors at hospitals | Uniform ~ [0,5] |

Table 29 summarizes the values of cost parameters used to demonstrate the proposed model. These values are obtained from Ensafian and Yaghoubi (2017), Barbee et al. (2015), and Gunpinar and Centeno (2015). Penalty cost for substituting one type of red blood cells for another blood type during transfusion is assumed to be 1% of unit production cost.

**Table 29. Cost parameters**

| Cost parameter | Value | Units | Reference |
|---|---|---|---|
| Fixed production cost | 1 | $/unit | Ensafian and Yaghoubi (2017) |
| Variable production cost | 150 | $/unit | Ensafian and Yaghoubi (2017) |
| Apheresis production cost (PLT) | 538 | $/unit | Barbee et al. (2015) |
| Apheresis production cost (RBC) | 219 | $/unit | Barbee et al. (2015) |
| Inventory holding cost | 1.25 | $/day*unit | Gunpinar and Centeno (2015) |
| Shortage cost | 1500 | $/unit | Gunpinar and Centeno (2015) |
| Outdating cost | 150 | $/unit | Gunpinar and Centeno (2015) |
| Transportation cost | 0.19 | $/mile*unit | Ensafian and Yaghoubi (2017) |

### 4.6.2. Numerical results

The stochastic program is solved using IBM ILOG CPLEX 12.8 on Dell OPTIPLEX 9020 computer running with 3.40 GHz CPU and 16GB of RAM. The proposed model has 3,876,255 constraints and 4,604,625 variables with 5 demand scenarios.

The proposed multi-product blood supply chain model considers production, inventory holding, transportation, substitution penalty, out shipping, shortage and outdate costs for both red blood cells and platelets. To achieve the lowest total cost, it is necessary to balance shortage and outdates for both products as well as balancing whole blood production and apheresis production considering the large demand difference between red blood cells and platelets. Table 30 summarizes the optimal daily cost that allows the model to satisfy both demand for red blood cells and platelets in all five scenarios within the 45-day planning period. Because daily cost during the third day to the forty-third day fluctuates up and down within a certain range, we use

the average value to show the numerical results. In addition, the fluctuation of total cost from day 3 to day 43 is shown in Figure 19. As can be seen in Figure 19, total cost ranges from $26,185 to $47,332 with a mean value of $36,095 during these days. There is a weekly pattern with peaks on Mondays. This is to be expected as mean demand is highest for Monday.

From Table 30, we can see that the minimum total cost for the multi-product blood supply chain is $1,713,537 during the planning horizon. This mainly comes from production cost which takes a proportion of approximately 96.27%. The production cost involves both whole blood and apheresis blood production costs of red blood cells and platelets and production cost for initial inventory. The average initial inventory is about 745 units for red blood cells and 120 units for platelets in all five demand scenarios. The number of red blood cells produced on average is 11,914 units with 23.99% from whole blood production. The total production of platelets on average is 3,784 units with 75.52% being derived from whole blood. There are nearly four times as many red blood cells being produced as platelets. For red blood cells, there are no outdates. Hence, all the units produced are used for fulfilling demand. While, for platelets, there are 92.4 units shipped out of the system to satisfy demand in other areas. This suggests that platelets are over produced. The over production of platelets is due to the demand difference between red blood cells and platelets and characteristic of whole blood production. As one unit of whole blood can produce one unit of red blood cells and one unit of platelets at the same time, the amount of whole blood derived red blood cells will equal the amount of whole blood derived platelets. On one hand, if this quantity is too small, there may not be enough red blood cells to satisfy demand and shortage occurs. On the other hand, if this quantity is too big, platelets are over produced. The optimal production is a tradeoff between shortages and outdates of red blood

cells and platelets separately as well as between shortages of red blood cells and over production of platelets.

The inventory holding cost is the second largest, about 1.73% of the total. This includes an additional one day holding cost for initial inventory of red blood cells and platelets. The quantity of total inventory is about 18,426 units for red blood cells and 4,487 units for platelets on average under all scenarios. Shortage cost is the third largest at 1.43%. Shortage for platelets is 10.2 units and occurs on the first day. Shortage for red blood cells is 6.1 units and mainly occurs on the second day with some on the third day. This is because satisfying demand on the first few days depends on the initial inventory as production takes at least one day. Transportation cost takes a relatively small percentage compared with other costs as unit transportation cost is very small in a local area. Outdate costs and substitution penalty costs are zero and are thus not shown in the table.

**Table 30. Results for daily cost of multi-product model**

| | **Production Cost** | **Holding Cost** | **Shortage Cost** | **Transportation Cost** | **Out shipping Cost** | **Total Cost** |
|---|---|---|---|---|---|---|
| Day 1 | 166,301 | 2,161 | 15,300 | 277 | - | 184,039 |
| Day 2 | 27,352 | 709 | 9,000 | 251 | 1 | 37,312 |
| 3-43 | | | | | | |
| Avg. | 35,242 | 631 | 4 | 206 | 11 | 36,095 |
| Day 44 | 11,101 | 828 | - | 219 | - | 12,148 |
| Day 45 | - | 133 | - | - | - | 133 |
| Total | 1,649,694 | 29,722 | 24,469 | 9,190 | 462 | 1,713,537 |

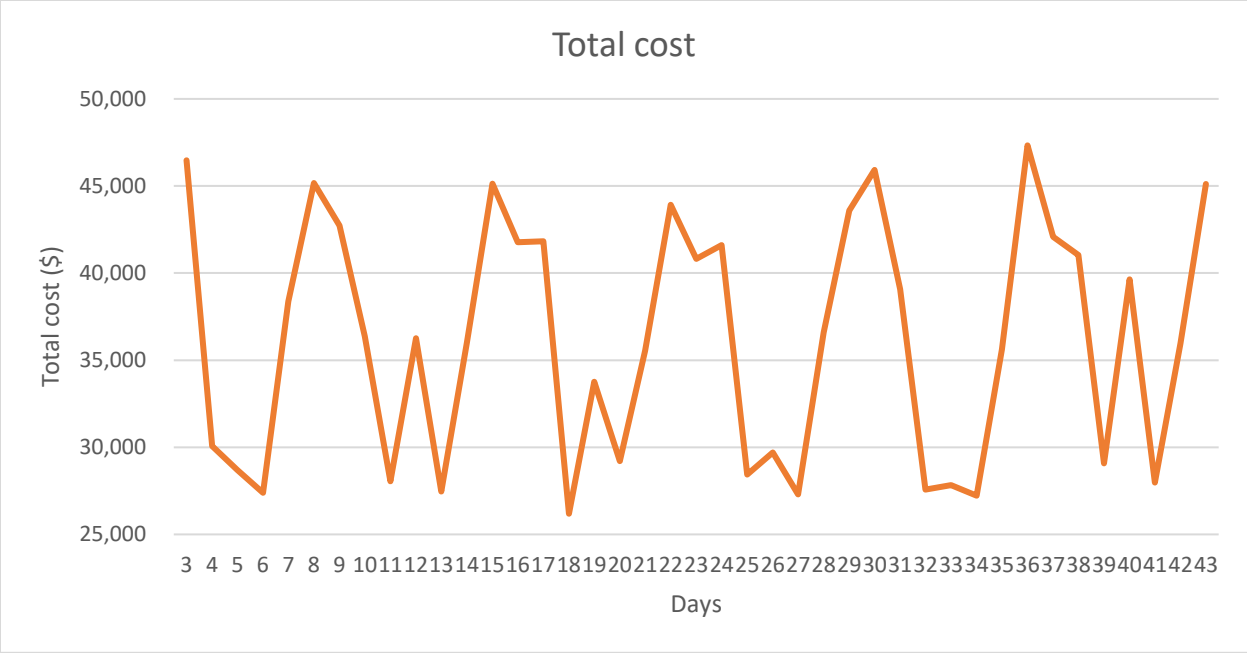


**Figure 19. Total cost between Day 3 and Day 43**

### 4.6.3. Comparing the multi-product model to an uncoordinated model

In this section, the proposed multi-product supply chain model is compared with an uncoordinated model which handles the red blood cell and platelet supply chains separately. First, the red blood cell supply chain is considered. Demand for red blood cells is the same as the multi-product model but demand for platelets is set to be zero. However, when producing red blood cells through whole blood, the same amount of platelets will also be produced and put into inventory. These platelets will stay in the inventory until they expire because of zero demand for platelets. We do not consider the holding and outdate costs for these platelets in the red blood cell supply chain. Instead, we add the quantity of whole blood derived platelets from the red blood cell supply chain to the inventory of the platelet supply chain on the corresponding days. For the platelet supply chain, demand for platelets is the same as the multi-product model while demand for red blood cells is set to be zero. In addition, available whole blood donors are also

set to be zero. According to previous research on the platelet supply chain (Xu & Szmerekovsky, 2019), we find that platelets only come from apheresis production instead of whole blood production.

Table 31 and Table 32 show results of daily cost for the red blood cell supply chain and corresponding platelet supply chain, respectively. The total cost is on average $1,508,088 for the red blood cell supply chain and $313,188 for the platelet supply chain in all five demand scenarios within the 45-day planning period. The two single product supply chains have similar cost distributions as the multi-product model where production cost takes over 90% of total cost. For the red blood cell supply chain, 11,914 units of red blood cells are produced and around 10.45% are derived from whole blood. At the same time, approximately 1,245 units of platelets are produced, and these units are put into inventory for the platelet supply chain. Therefore, the whole production cost is only considered in the red blood cell supply chain to avoid double counting. For the platelet model, an additional 2,535 units of platelets are produced through apheresis. As there are three different demand types for platelets and only apheresis derived platelets are "fresh", it is necessary to produce enough platelets through apheresis to avoid shortage. Like the multi-product model, platelets are also over produced as the quantity of platelets shipped out of the system is 72.4 units.

**Table 31. Results for daily cost of the red blood cell supply chain**

| | **Production Cost** | **Holding Cost** | **Shortage Cost** | **Transportation Cost** | **Total Cost** |
|---|---|---|---|---|---|
| Day 1 | 139,210 | 1,864 | - | 187 | 141,261 |
| Day 2 | 27,947 | 600 | 9,000 | 240 | 37,787 |
| 3-43 Avg. | 31,364 | 549 | 4 | 139 | 32,056 |
| Day 44 | 13,781 | 698 | - | 142 | 14,621 |
| Day 45 | - | 114 | - | - | 114 |
| Total | 1,466,867 | 25,779 | 9,169 | 6,273 | 1,508,088 |

**Table 32. Results for daily cost of the platelet supply chain**

| | Production Cost | Holding Cost | Shortage Cost | Transportation Cost | Out shipping Cost | Total Cost |
|---|---|---|---|---|---|---|
| Day 1 | 28,000 | 295 | 15,300 | 35 | - | 43,629 |
| Day 2 | 14,503 | 120 | - | 20 | 18 | 14,660 |
| 3-43 Avg. | 6,047 | 130 | - | 26 | 8 | 6,211 |
| Day 44 | - | 149 | - | 47 | - | 196 |
| Day 45 | - | 38 | - | - | - | 38 |
| Total | 290,447 | 5,924 | 15,300 | 1,155 | 362 | 313,188 |

To examine the differences between the multi-product model and the uncoordinated model, it is necessary to sum up the results for the red blood cell and the platelet supply chains and compare it to the multi-product model under different realized demand within the 45-day planning horizon. Therefore, we select production cost, holding cost, shortage cost, transportation cost, out shipping cost, and total cost as performance measurements, and perform an analysis on ten groups of demand data that are randomly generated from the varying daily mean value on each day of the week. Each group of demand data includes five demand scenarios for five hospitals in 45 days. In order to evaluate whether the numerical results obtained from the multi-product model are significantly different from that of the uncoordinated model, we conduct a paired sample T-test on total costs for both models. Our result indicates that there is a statistically significant difference between the means of total cost for the multi-product model and sum of single product supply chains (p-value = 0.000 < 0.05).

Table 33 shows the comparisons of different costs for the multi-product model and sum of single product supply chains, where the results are the averages on ten groups of demand data. The total cost for the multi-product model is $1,704,291, while it is $1,810,950 for the uncoordinated model, an increase of 6.26%. A coordinated multi-product model can save $106,659 in 45 days, that is about $0.87 million annual savings. The cost difference between

both models mainly comes from differences in production cost. The number of red blood cells produced in both models is the same and the number of platelets produced by the multi-product model is only 2 units more than that of the uncoordinated model. However, the total production cost for the multi-product model is significantly lower than the uncoordinated model. This suggests that average unit production cost is lower for the multi-product model. Both red blood cells and platelets can be produced through whole blood and apheresis. One unit of whole blood can produce one unit of red blood cells and one unit of platelets. One apheresis production can obtain two units of red blood cells or five units of platelets. Using cost parameters stated in Table 29, we find that unit apheresis production cost is $109.5 (219/2) for red blood cells, and $107.6 (538/5) for platelets. Things are more complicated for whole blood production. For the multi-product model, unit production cost is considered as $75 (150/2) since one unit of whole blood can produce two units of blood products. But for the uncoordinated model, unit production cost is $150 for the red blood cell supply chain and $0 for the platelet supply chain. Therefore, whole blood production is a preferred approach for the multi-product model ($75 < $107.6 < $109.5), but apheresis production is a preferred approach for the uncoordinated model ($107.6 < $109.5 < $150). Our results verify this conclusion as the ratio of whole blood derived red blood cells to total produced red blood cells is 23.83% for the multi-product model and 10.76% for the red blood cell supply chain. This explains why average unit production cost for the multi-product model is lower than the uncoordinated model. In addition to production cost, inventory holding cost also increases by 5.66% for the uncoordinated model. Although the average daily inventory for platelets is almost the same, the average daily inventory for red blood cells is 452 units for the uncoordinated model compared to 411 units for the multi-product model. From these results,

we can conclude that considering a coordinated multi-product model is important in reducing production and inventory holding costs for the blood supply chain.

**Table 33. Comparisons of different costs for multi-product model and sum of single product supply chains**

| | Multi-product | Sum of single product | Change |
|---|---|---|---|
| **Production cost** | 1,652,158 | 1,758,752 | 6.45% |
| **Holding cost** | 30,817 | 32,560 | 5.66% |
| **Shortage cost** | 11,763 | 11,763 | 0.00% |
| **Transportation cost** | 9,210 | 7,546 | -18.07% |
| **Out shipping cost** | 343 | 330 | -3.91% |
| **Total cost** | 1,704,291 | 1,810,950 | 6.26% |

### 4.6.4. Sensitivity analysis

As total cost for the red blood cell supply chain is much higher than the cost for the platelet supply chain, changing the supply of red blood cells should significantly influence the performance of both the coordinated and uncoordinated blood supply chains. In this section, we perform sensitivity analysis to explore the impacts of donors on system performance with total cost as the performance indicator. First, we examine the influence on total cost by changing the number of both whole blood donors and apheresis donors for red blood cells. Second, we explore the impact on total cost by only altering the number of apheresis donors for red blood cells. Third, the impact of changing available whole blood donors is investigated.

#### *4.6.4.1. Impact of changing both whole blood and apheresis RBC donors*

To evaluate the impact of changing both whole blood and apheresis RBC donors on total cost, we consider three different situations: decreasing supply of red blood cells by multiplying by 0.8, the base case, and increasing supply by multiplying by 1.2. Table 34 shows the average total cost for the multi-product model and two single product supply chains under these three situations with 10 different groups of demand data. When the supply of red blood cells decreases

from 1 to 0.8, total cost for the multi-product model increases by 28.02%. However, total cost for the red blood cell supply chain increases by 35.41% and decreases by 51.24% for the platelet supply chain, which leads to an increase of 21.01% in total cost for the uncoordinated model. The increases on total cost mainly come from shortages of red blood cells for both models. As there exist shortages and the quantity of shortages are the same, the cost difference between the two models decreases to 0.44%. When the supply of red blood cells increases from 1 to 1.2, total cost for the multi-product model decreases by 0.8%. However, total cost for the uncoordinated model increases because the cost increase for the platelet supply chain exceeds the cost decrease for the red blood cell supply chain. This can be explained by the fact that a larger number of available donors will result in more units of red blood cells produced through apheresis and less whole blood production for the red blood cell supply chain, thus increasing the production of platelets through apheresis for the platelet supply chain. The cost difference between the multi-product model and the uncoordinated model enlarges to 10.84%. These results suggest that a coordinated multi-product blood supply chain performs much better than an uncoordinated single product supply chain as the number of donors increases.

**Table 34. Comparisons of total cost for multi-product and uncoordinated models under different numbers of donors**

| | | Single product | | | |
|---|---|---|---|---|---|
| **Donor multiples** | **Multi-product** | **RBC** | **PLT** | **Sum** | **Change** |
| **0.8** | 2,181,755 | 2,044,706 | 146,734 | 2,191,440 | 0.44% |
| **1** | 1,704,291 | 1,510,025 | 300,926 | 1,810,950 | 6.26% |
| **1.2** | 1,690,732 | 1,452,392 | 421,665 | 1,874,056 | 10.84% |

#### *4.6.4.2. Impact of changing available apheresis RBC donors or whole blood donors*

As red blood cells can be obtained from both whole blood donors and apheresis RBC donors, it is useful to identify which type of donor has a higher impact on system performance.

The impact of available apheresis donors of red blood cells on total cost is examined through multiplying the number of total apheresis RBC donors by 0.8, 1, and, 1.2 respectively. The corresponding average result of total cost for the multi-product model and two single product supply chains under 10 groups of demand data is shown in Table 35. The result is quite similar to the previous sensitivity analysis on both whole blood and apheresis RBC donors except that quantity of blood shortage is smaller when decreasing supply. It looks like apheresis donors of red blood cells have a major influence on the cost efficiency of the blood supply chain. To verify this, we also checked the impact of whole blood donors on total cost.

Similarly, we multiply the number of whole blood donors by 0.8, 1, and 1.2 respectively, and then conducted experiments on the multi-product model and two single product supply chains with 10 groups of demand data. Table 36 shows the comparisons of total cost for both models under different numbers of whole blood donors. When the number of whole blood donors increases, changes on total cost for both the multi-product model and sum of single product supply chains are negligible. This indicates that changes in whole blood donors do not have much impact on total cost.

In summary, a coordinated multi-product blood supply chain is better at leveraging larger numbers of donors. The cost savings over uncoordinated single product supply chains mainly come from variations in the number of apheresis RBC donors.

**Table 35. Comparisons of total cost for multi-product and uncoordinated models under different numbers of apheresis donors**

| | | Single product | | | |
|---|---|---|---|---|---|
| **Apheresis multiples** | **Multi-product** | **RBC** | **PLT** | **Sum** | **Change** |
| **0.8** | 1,822,405 | 1,688,268 | 140,232 | 1,828,500 | 0.33% |
| **1** | 1,704,291 | 1,510,025 | 300,926 | 1,810,950 | 6.26% |
| **1.2** | 1,692,215 | 1,452,399 | 421,673 | 1,874,071 | 10.75% |

**Table 36. Comparisons of total cost for multi-product and uncoordinated models under different numbers of whole blood donors**

| | | Single product | | | |
|---|---|---|---|---|---|
| **Whole blood donor multiples** | **Multi-product** | **RBC** | **PLT** | **Sum** | **Change** |
| **0.8** | 1,706,970 | 1,510,611 | 299,458 | 1,810,068 | 6.04% |
| **1** | 1,704,291 | 1,510,025 | 300,926 | 1,810,950 | 6.26% |
| **1.2** | 1,702,663 | 1,509,793 | 302,152 | 1,811,945 | 6.42% |

## 4.7. Conclusion

This paper presents a multi-product multi-period stochastic program for an integrated blood supply chain which includes two perishable blood products. The blood supply chain consists of one regional blood center, several blood collection sites and hospitals with consideration of demand uncertainty, age information of blood products, blood type substitution of red blood cells, three demand types of platelets, and centralized operational decisions. The aim of the model is to minimize the total cost incurred during the collection, production, inventory, and distribution by making optimal decisions on the quantity of collected whole blood and apheresis derived red blood cells and platelets, the quantity of whole blood separation, and the quantity of blood distribution to different hospitals. In the multi-product system, the RBC and PLT supply chains intertwine at the collection and production stages as whole blood donated can be separated into red blood cells and platelets at the same time. The sharing of a production process and the demand differences between red blood cells and platelets may result in excess platelets that can't be absorbed by the current supply chain system and have to be distributed to other blood supply chains.

The formulated model was applied to a real case study from the Fargo-Moorhead area, North Dakota and Minnesota, USA. The results were analyzed and compared with that of an uncoordinated model where the red blood cell and platelet supply chains were considered

separately. Our numerical result for the multi-product model indicated that production cost takes over 90% of overall cost and optimal decision on production is a tradeoff between shortages and outdates of red blood cells and platelets separately as well as between shortages of red blood cells and over production of platelets. We also found that a coordinated multi-product model outperforms an uncoordinated model, and coordinating decisions can save $106,659 within a 45-day planning period, that is about $0.87 million annual savings. Furthermore, sensitivity analyses were implemented to explore the impacts of whole blood donors and apheresis donors for red blood cells on system performance of both coordinated and uncoordinated supply chains. The analysis showed that the coordinated multi-product model performs much better than an uncoordinated model as the number of donors increases and these cost savings mainly come from changes in the number of apheresis donors. Changes in the number of whole blood donors do not have much impact on total cost, but it is notable that an increase in whole blood donors can hurt the performance of the supply chain if a multi-product model is not used to coordinate production of red blood cells and platelets.

There are several future research directions. First, developing efficient solution algorithms to solve a large-scale problem within a reasonable time. It takes more than one hour to get a solution for the formulated problem, and the computational complexity increases dramatically if considering more facilities sites and hospitals or a longer time horizon. Second, the consideration of a larger blood supply chain with more blood centers, collection sites and hospitals. It is normal to have multiple blood centers in large cities such as New York and it is necessary to consider the interactions among these blood centers. Third, considering weekends and holidays when normal blood collection and production activities are not conducted.

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