PLATELET INVENTORY MANAGEMENT IN BLOOD SUPPLY CHAIN UNDER DEMAND AND SUPPLY UNCERTAINTY

A Dissertation

presented to

the Faculty of the Graduate School

at the University of Missouri-Columbia

In Partial Fulfillment

of the Requirements for the Degree

Doctor of Philosophy

---

by

Han Shih

Dr. Suchithra Rajendran, Dissertation Supervisor

July 2021

The undersigned, appointed by the dean of the Graduate School, have examined the dissertation entitled

PLATELET INVENTORY MANAGEMENT IN BLOOD SUPPLY CHAIN UNDER DEMAND AND SUPPLY UNCERTAINTY

presented by Han Shih, a candidate for the degree of doctor of philosophy, and hereby certify that, in their opinion, it is worthy of acceptance

Dr. Suchithra Rajendran, Committee Chairperson

Dr. Luis Occena, Committee Member

Dr. Kangwon Seo, Committee Member

Dr. Zezong Gu, Committee Member

DEDICATION

This dissertation is dedicated in memory of my parents for their love and support throughout my life. Due to the foreign wars and civil wars, my parents didn’t have opportunities to get a good education, but they taught me how to be a down-to-earth and responsible person. Their tremendous sacrifices have allowed me to get a better education. Thank you, my dear parents.

ACKNOWLEDGEMENTS

The IMSE PhD program at the University of Missouri Columbia has been a challenging and rewarding journey for me, both academically and emotionally. I thank my God for giving me the opportunity to carry through my PhD program after I retired from MIZZOU, and for letting me through all the difficulties.

First and foremost, I am incredibly grateful to my advisor, Professor Suchithra Rajendran, for her invaluable advice, continuous support, constant guidance, and patience during my PhD study and research. She has been supportive in every way since the days I began working on my thesis as a PhD student, and her expertise, support and guidance encouraged me to pursue my research in my area of interest. Her advice both on my research as well as on my career has been invaluable. Thank you, Dr. Suchi.

I would like to express my sincere gratitude and appreciation to my committee members, Professor Luis Occena, Professor Kangwon Seo, and Professor Zezong Gu for serving as my committee members and many thanks to them for spending their valuable time to provide brilliant comments and suggestions during my PhD comprehensive exam.

I want to give thanks to Professor Luis Occena for encouraging me to complete my PhD degree after I retired from MIZZOU. During my first year as PhD student, I was thinking about quitting; my advisor Professor Suchithra Rajendran and Professor Luis Occena strongly encourage me not to leave the PhD program. I sincerely thank them for their encouragement and confidence in me and I am determined to achieve my goal.

I would also like to acknowledge my friends, colleagues, and loved ones who made my doctoral journey possible; special thanks to my colleague IMSE PhD candidate, Akhouri Amitanand Sinha, whose assistance allowed my thesis to go the extra mile.

Some funding sources have allowed me to pursue my PhD studies. I am grateful to the US Department of Education for funding my PhD study through the Graduate Assistance in Areas of National Need (GAANN) fellowship. I would also like to express my deep gratitude to Professor James Noble for providing me the privilege of working under Professor Bin Wu as a graduate teaching assistant and an excellent teaching assistant experience.

During the course of my research work, I am very grateful to Kuan-Tsou (Johnny) Lin, Director of the Department of Operation, and Ming-Chang Lin, Director of Hsin Chu Blood Center at the TBSF (Taiwan Blood Services Foundation), for providing valuable data for my research. I would also like to show my gratitude to Sabrina Lei Li, Director of the Department of Public Relations, who provides essential insight and expertise that greatly assisted my research.

I am humbled and thrilled to receive the award as the Outstanding IMSE PhD Student for 2021. I am very grateful to the faculty of the IMSE department for their constant help and support.

"Love never fails" – I would like to express my special appreciation and thanks to my wife, Chia Li, my son, Alex, my daughter-in-law, Naomi, my daughter, Grace, and my son-in-law, Peter. Without their tremendous understanding, support, and encouragement in the past few years, it would be impossible for me to complete my PhD study. Their prayers for me were what gave me strength and sustained me thus far.

TABLE OF CONTENTS

LIST OF ILLUSTRATIONS

LIST OF TABLES

ABSTRACT

Supply chain management of blood and its products are of paramount importance in medical treatment due to its perishable nature, uncertain demand, and lack of auxiliary substitutes. For example, the Red Blood Cells (RBC's) have a life span of approximately 40 days, whereas platelets have a shelf life of up to five days after extraction from the human body. According to the World Health Organization, approximately 112 million blood units are collected worldwide annually. However, nearly 20% of units are discarded in developed nations due to being expired before the final use. A similar trend is noticed in developing countries as well. On the other hand, blood shortage could lead to elective surgeries cancellations. Therefore, managing blood distribution and developing an efficient blood inventory management is considered a critical issue in the supply chain domain.

A standard blood supply chain (BSC) achieves the movement of blood products (red blood cells, white blood cells, and platelets) from initial collection to final patients in several echelons. The first step comprises of donation of blood by donors at the donation or mobile centers. The donation sites transport the blood units to blood centers where several tests for infections are carried out. The blood centers then store either the whole blood units or segregate them into their individual products. Finally, they are distributed to the healthcare facilities when required.

In this dissertation, an efficient forecasting model is developed to forecast the supply of blood. We leverage five years' worth of historical blood supply data from the Taiwan Blood Services Foundation (TBSF) to conduct our forecasting study. With the generated supply and demand distributioins from historial supply and demand data as inputs, a single objective stochastic model is developed to determine the number of platelet units to order and the time between orders at the hospitals. To reduce platelet shortage and outdating, a collaborative network between the blood centers and hospitals is proposed; the model is extended to determine the optimal ordering policy for a divergent network consisting of multiple blood centers and hospitals. It has been shown that a collaborative system of blood centers and hospitals is better than a decentralized system in which each hospital is supplied with blood only by its corresponding blood center. Furthermore, a mathematical model is proposed based on multi-criteria decision-making (MCDM) techniques, in which different conflicting objective functions are satisfied to generate an efficient and satisfactory solution for a blood supply chain comprising of two hospitals and one blood center.

This study also conducted a sensitivity analysis to examine the impacts of the coefficient of demand and supply variation and the settings of cost parameters on the average total cost and the performance measures (units of shortage, outdated units, inventory holding units, and purchased units) for both the blood center and hospitals.

The proposed models can also be applied to determine ordering policies for other supply chain of perishable products, such as perishable food or drug supply chains.

Keywords: Blood Supply Chain; Perishable Products; Wastage; Shortage; Time Series Forecasting Methods; Machine Learning Algorithms; Stochastic Integer Programming Models, Multi-Criteria Decision-Making Approaches, Goal Programming.

CHAPTER 1
INTRODUCTION

1.1 Background

"A Supply Chain (SC) consists of all parties involved, directly or indirectly, in fulfilling a customer request. The supply chain includes not only the manufacturer and suppliers, but all transporters, warehouses, retailers, and customers themselves. A supply chain is dynamic and involves the constant flow of information, product, and funds between different stages" (Chopra and Meindl, 2007). Supply chain management defines concepts regarding integrated business planning that has been supported by strategists, logistics experts, and operations research practitioners (Shapiro, 2001). According to the American Production and Inventory Control Society Dictionary (2016), Supply Chain Management (SCM) effectively designs, plans, executes, and controls all activities committed to sourcing and acquisition, transformation, and management of supply chain tasks to achieve the goal of enhancing the net value.

The general supply chain system consists of suppliers and vendors, producing centers, storage warehouses, distribution centers, and retail stores. In each of these stages, many have unfinished inventories and finished goods that involve the process flow of works between the facilities (Simchi-Levi et al., 2000; Nagurney, 2012). According to Nagurney (2006), "supply chains are the critical infrastructure for the production, distribution, and consumption of products as well as services in our globalized network economy".

Supply chains that deliver perishable items, such as blood, medicines, food, biological drugs, and vaccines, have addressed the particular challenges that many companies face. A perishable item, by definition, has a fixed lifespan, and ought to be discarded after that duration has passed. Every element of blood always perishes within a different time. The platelet, one of the critical components of blood, has only a five-day shelf life; whereas red blood cell (RBC) has 42 days, and plasma and cryoprecipitate have a shelf life of one year each (Prastacos, 1984; Osorio et al., 2015; Ekici et al., 2017). The short life of blood items requires an in-depth linkage between stock inventory and immediate planned use (Mulcahy et al., 2016). Figure 1.1 shows a typical blood supply chain (Mulcahy et al., 2016).

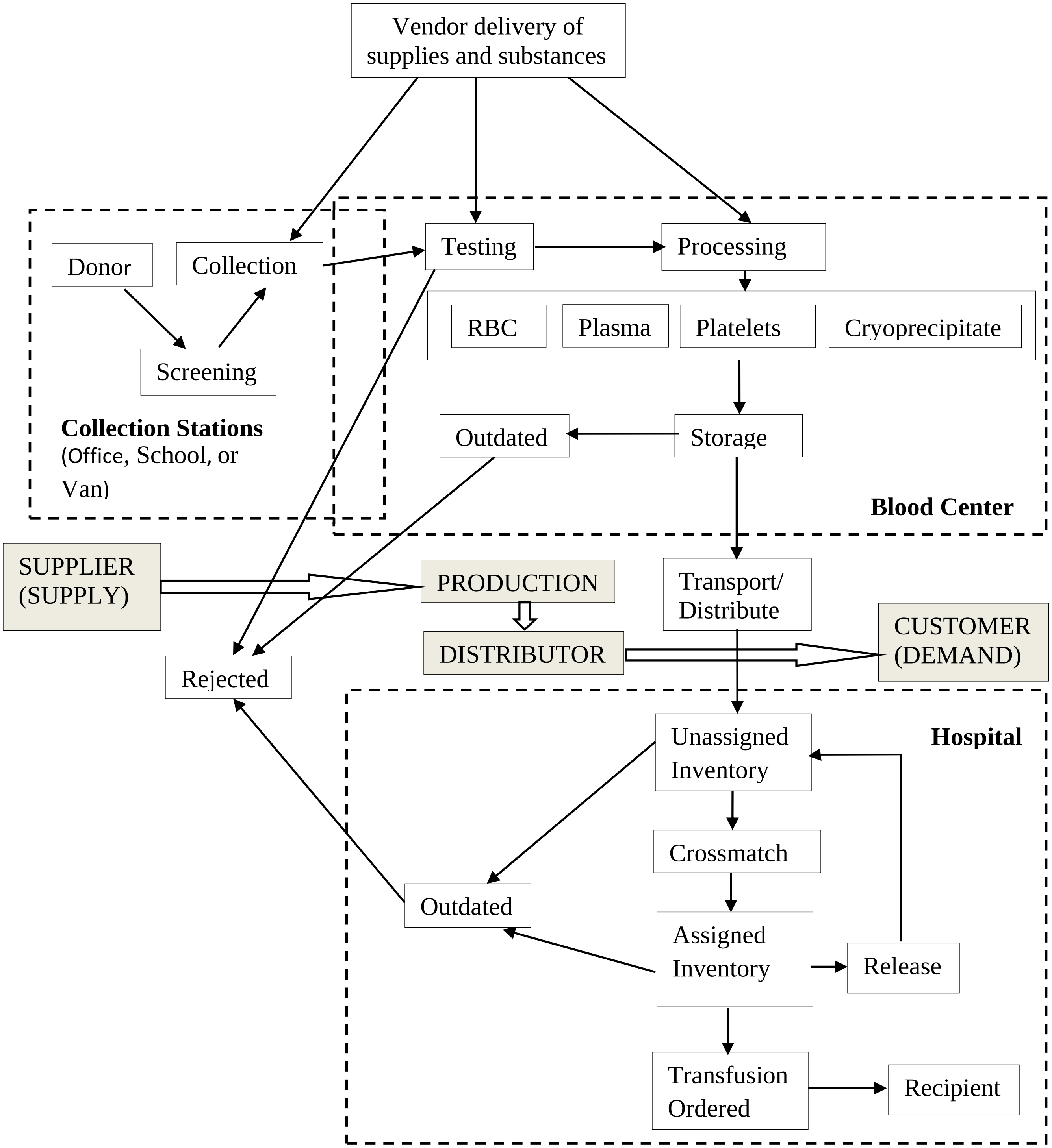


Figure 1.1: Typical Blood Supply Chain (Adapted from Mulcahy et al., 2016)

1.2 Blood: The Basics

Blood performs many necessary functions within the physical body like transporting nutrients, oxygen and chemicals to different cells and tissues in the body, squandering expulsion, battling against infections, regulating the physique temperature, and regulating body acidity (Lowalekar and Ravichandran, 2015; Albdulwahab, 2015). Blood is an active tissue or cell of different medical amounts in the human body. Within the US population, blood appears in eight major blood whose frequencies differ from 38% (O+) to 0.5% (AB-). It is made up of different constituents, including assorted types of white cells, red cells, plasma, and platelets, many of which could be commonly separated from the whole blood itself.

1.2.1 Blood Components and their Functions

Nearly 7-8% of the human body weight is due to blood. This essential liquid does the primary activity of transporting oxygen and supplements to cells of our body and disposing of ammonia, carbon dioxide, and other waste items. Additionally, it plays a significant role in our system in maintaining a comparatively constant body temperature (Wangboon et al., 2017). The process of withdrawing one or more blood components from a donor is known as apheresis. White blood cells, red blood cells, plasma, and platelets are four of the most critical blood components.

- Red Blood Cells (RBCs, also known as Erythrocytes)

Red blood cells are the first abounding cell within the blood, representing around 40 - 45% of its volume. They are created in the bone marrow and contain an oxygen carrier protein called hemoglobin, which helps transport oxygen from the lungs to other parts of the body, and returns carbon dioxide from the body to the lungs so that it can be breathed out (American Society of Hematology, 2018).

- White blood cells (WBCs , also called Leukocytes)

They are an essential part of the immune system and abort infectious agents referred to as pathogens. Granulocytes, lymphocytes, and monocytes are the three main kinds of white blood cells, which defend the body against infection. They represent around 1% of blood volume, and the number is much less than red blood cells. Once viruses or microorganisms enter the blood, for instance, through a cut, a scratched knee, or a contaminated ear, white blood cells destroy the incursive microorganisms (American Society of Hematology, 2018).

- Platelets (also called Thrombocytes)

Different from red and white blood cells, platelets are tiny, delicate, plate-shaped cell fragments. Platelets facilitate the blood clotting process by forming a platform that seals the wound and forestalls the loss of blood (American Society of Hematology, 2018).

- Plasma

Plasma is the straw-shaded fluid segment of blood, a blend of water, sugar, fat, protein, and salts (electrolytes). Around 90% of plasma is water, and the other 10% is formed from the different materials which are delivered by the plasma. Plasma acts as a transit for the matrix within the blood. Plasma provides all parts of the human body with supplements such as proteins, minerals, vitamins, sugars, fats, and diverts waste products items (Prastacos, 1984). Plasma likewise transports red blood cells and carbon dioxide to and back from our organs and tissues.

1.2.2 Blood Types and Blood Matches

Blood has eight standard types. Specific antigens will trigger an immune reaction if they do not belong to the human body, and these antigens' absence or presence determines blood varieties. Because some antigens will prompt a patient's immune system to attack the transfused blood; therefore, transfusions of safe blood rely upon watchful blood composing and cross-matching (American Red Cross, 2018).

Regarding blood transfusions, matching blood types is the process for compatibility testing between the donor’s blood and the recipient's blood. Cross-matching generally does not mean an identical blood match. Table 1.1 shows the distribution of red blood cell types and all possible suitable substitutions for ABO/Rh (D) in the US Population (Duan and Liao, 2014).

Table 1.1: Distribution of Red Blood Cell Types and all possible suitable substitutions for ABO/Rh (D) (Duan and Liao, 2014).

Blood Cell type	Blood Type Compatibility							
	O+	O-	A+	A-	B+	B-	AB+	AB-
O+	√		√		√		√	
O-	√	√	√	√	√	√	√	√
A+			√				√	
A-			√	√			√	√
B+					√		√	

Blood Cell type	Blood Type Compatibility							
	O+	O-	A+	A-	B+	B-	AB+	AB-
B-					√	√	√	√
AB+							√	
AB-							√	√

1.3 Blood Supply Chain

Figure 1.2 outlines the blood supply chain network and the flows among the stages (Osorio et al., 2015).

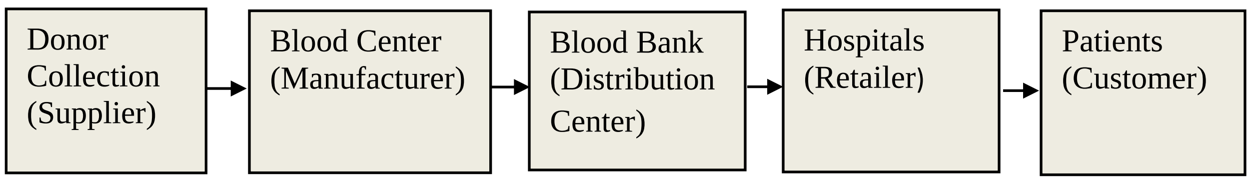


Figure 1.2: Flow of the Elements within the Blood Supply Chain (Adapted from Osorio et al., 2015)

The blood supply chain and its segments from donation to transfusion are from various perspectives, like a conventional logistic supply chain. This is a planned activity where the blood units are collected, processed, and separated into parts, stored, transported, and transfused.

The stochastic character of both blood demand and supply makes the management of the blood supply chain, particularly challenging (Jennings, 1973; Rajendran and Ravindran, 2017). Lead time is not easy to forecast because it is attributable to the uncertainty associated with the number of donations, blood classification, and processing time.

- Donor Collection (Supplier)

The first blood supply chain segment is blood donation. In the US, blood is collected from blood donors by many institutions and arrangements; all of the institutions should be registered and obtain licenses from the US Food and Drug Administration (FDA) (Mulcahy et al., 2016).

Blood units are gathered from settled blood facilities or via temporary ones. After the enrollment procedure, all the donors who visit the blood facilities are subjected to a screening procedure to abstain from transmitting diseases through blood transfusion.

- Blood Center - Manufacturer

A blood center is a facility set up to involve in collecting blood from donors, test, process, and store blood and its components for use in the future. The essential duty for each blood center is to set up blood assortment and respond promptly to the patients' requests for blood and its components. Blood centers get orders from their distributed hospitals or medical centers, according to the anticipated needs of blood (Khanghahi et al., 2018). Every vehicle begins from a blood center and returns to the same blood center after exploring a designated route to serve selected hospitals (Khanghahi et al., 2018).

Any blood center has main objectives: (a) to minimize blood wastage and (b) to guarantee those blood items are accessible in adequate amounts for patients who require blood transfusion (Jennings, 1973; Lowalekar and Ravichandran 2015).

Apheresis or the process of extracting a particular part of the blood, like platelets, with the remaining constituents such as plasma and red blood cells returning to the blood donor, is a progressively common procedure. This method permits a significant amount of one specific part of the collected blood, which could be separated from a unit of whole blood (American Association of Blood Banks, 2018).

- Blood Bank (Storage and Inventory - Warehouse and Distribution)

After the blood is tested, processed, and available for transfusion, the blood needs to be transported, stored, and recorded before use. The FDA also provides regulations on the requirements of blood storage to guarantee safety throughout its life cycle (Mulcahy et al., 2016). Blood would need to be discarded before transfusion due to the following reasons: (1) time expiration (Various blood component units exceeding their different shelf life), (2) refrigerator malfunction (e.g., due to power outage, equipment failure), (3) exceeding timeframe of refrigeration temperature (units moved out of refrigeration exceeding a specified timeframe that cannot be returned to the main stock) and (4) other different wastage situations (e.g., dropping blood, damaging to its packaging) (Stanger et al., 2012; Mulcahy et al., 2016). Platelets have five to seven days to be used before they perish and need to be discarded; its deterioration is usually faster than the deterioration of other blood components.

- Hospitals (Crossmatching) - Retailer, Store

The purpose of cross-matching is to examine the compatibilities of the donor's and recipient's blood, and the blood the recipient could receive from the inventory (Pierskalla, 2005). The Hospital blood center functions as an inventory location, which is to store and distribute units of blood to fulfill requests for transfusion. Throughout the day, the hospitals or medical centers receive irregular requests of transfusion for every blood group. The proper number of units of that type is taken out from available inventories. After successful cross-matching, those units are located on reserve inventory for a particular patient (Prastacos, 1984; Figure 1.1). Cross-matched blood is held in reserve for patients for a specific amount of time. Any units that are not transfused (generally within a day or two) are placed back to the free inventory. Crossmatch release period is the time between the patient's operation and the return back to the free inventory from the unused unit and has a considerable effect on the wastage (Prastacos, 1984; Ekici et al., 2017).

- Patients (Blood Transfusion) - Customer

A blood transfusion is a process through which the patient receives blood directly into one of the patient's blood vessels through an intravenous (IV) line. These procedures replace blood when blood is lost because of severe injuries or during surgeries. A transfusion may also be performed if one person's body cannot properly produce blood, due to sickness. Each year, almost 5 million people in the United States need blood transfusions (National Heart, Lung, and Blood Institute, 2018). In 2006, it was reported that the requests for blood transfusions are over 30 million units of blood components (American Association of Blood Banks, 2007). Increased life expectancy due to advanced progress in the medical procedures, the need for blood transfusions, and the rate of using blood products will arise (Davey, 2004; American Association of Blood Banks, 2018).

Yates et al. (2017) underlined that inventory management of blood is both challenging and crucial, guaranteeing accessibility while simultaneously limiting wastage. Because of the character of the blood supply, wastage of blood is a universal economic issue to be resolved, as the blood is collected only voluntarily in several countries. Management in blood inventory is thus a tradeoff, guaranteeing 100% accessibility of all types of blood and its components, in the least time, while minimizing wastage.

1.4 Current Issues in the Blood Supply Chain

Blood and its components are all required in a variety of treatments, including cancer treatments, organ transplants, major surgical operations, and trauma care. Around the world, people who need blood can die from insufficient blood product supply (World Health Organization, 2016). Even though substantial research has led to alternatives for blood, these endeavors have not been very fruitful yet. In 2013, it was reported that in the United States, there are around 15.2 million blood donors, roughly 14.2 million units of blood were gathered, out of which, 13.2 million units were transfused (Mulcahy et al., 2016).

- Better Blood Inventory Management

Hospitals and blood centers face challenges in managing blood inventory. To satisfy both anticipated and unexpected requests for blood, it is required to hold sufficient stock, while limiting waste. Lack of adequate inventory management practices is causing high costs for blood centers and hospitals, and the broader health care system. To effectively facilitate the inventory management of blood, hospitals depend on various kinds of tools, which include staff ability, internal management software package, and external inventory management, etc. American Red Cross reports the following facts about blood demand in the United States (American Red Cross, 2018):

- Nearly 10,000 units of plasma and 7,000 units of platelets are required every day within the United States.
- The daily need for RBCs is approximately 36,000 units within the United States.
- Every year, 90,000 to 100,000 individuals in the United States are influenced by sickle cell disease (SCD); nearly 1,000 infants get this disease when they were born. Sickle cell patients possibly require blood transfusions for their lives.
- The most frequently requested blood type by hospitals is type O
- By 2017, about 1.7 million individuals are predicted to receive a cancer diagnosis. In some cases every day, a large number of patients will require blood during their chemotherapy treatment.
- At least 100 pints of blood will be needed for a single automotive accident victim.
- Every year donors in the US donate about 13.6 million whole blood and RBCs.
- About 45% of individuals within the US have either positive or negative Group type O blood; African Americans (51%) and Hispanics (57%) have higher percentages.

- There are just 3% of individuals within the US population have AB positive blood. The AB-positive plasma can be transfused to all blood types of compatible recipients; its supply is limited.
- Type O negative red blood cells can be transfused to all blood types of compatible recipients. In the US, since just 7% of individuals are type O negative, it is dependable in the unusual request, and the supply is often in shortage.
- Red blood cells must be utilized no more than 42 days (or less).
- Platelets must be utilized for no more than five days.

  Moreover, both blood demand and supply are stochastic and are hard to control. A more robust blood inventory management is thus required.

- Importance of Forecasting

Reserving too many units of blood on an inventory might lead to this limited resource being wasted due to its perishability. However, shortages could lead to critical health-related cancellations and could trigger possible increases in the number of deaths in hospitals. Hence, accurate forecasting of blood demand and supply is essential to use this limited resource prudently. Management of blood demand and supply is regarded as a significant part of supply chain management in healthcare, and blood components are demanded to satisfy the requirement of their regular and irregular patients. Forecasting blood demand is essential for effective and well-structured planning of a blood supply chain (Filho et al., 2013). Predicting the demand and supply of blood components significantly impacts the main decisions made in blood supply chain inventory management.

Blood shortages will increase fatality rates for various groups and cause high societal prices (Beliën and Force, 2012). Hence, good blood inventory management is extraordinarily important.

- Emergency Blood Demand-Side Shocks

According to Butch (1985), an emergency is one of the internal factors that affect how well the blood bank inventory management performs. Recent disasters have shown that the blood supply chain and its effectiveness of operation services are plagued by external disruption (Jabbarzadeh et al., 2014). Certain types of major disasters that affect transfusion service are earthquakes, floods, terrorism, and biological events (Zaheer and Waheed, 2016). For instance, in the case of the Bam earthquake of December 2003, in southeastern Iran, only 23% of donated blood units were distributed to the troubled areas (Abolghasemi et al., 2008). Similarly, the blood supply chain was disturbed by the Sichuan earthquake in China in 2008 (Sha and Huang, 2012). The study of the London transit system terror attacks at rush hour in 2005 showed that the required 440 units of red cells (RCs) were needed and any future incidents in which the victims were involved and suffered major hemorrhages needed plasma, cryoprecipitate, and platelets (Glasgow et al., 2012). The 2011 Japanese earthquake and tsunami, the Great Sendai Earthquake, required 1,938 units of RBCs (Quillen and Luckey, 2014), and after the earthquake, the national blood collection and distribution system in Japan reacted adequately to the local requirements of blood allocation (Nollet et al., 2013). The 9/11 terrorist attacks needed an additional requirement of 258 units of blood, which was mainly provided by the hospitals with stock availability (Schmidt, 2002). In summary, over 475,000 blood units were collected for disaster victims, but only 258 units were used (Schmidt, 2002), and an estimated 250,000 units nationwide were disposed of (US General Accounting Office, 2002).

The study of mass loss and disaster incidents before the 9/11 terror attacks have indicated the patterns of the need for actual blood allocation (Schmidt, 2002). It is worth considering that though donations do tend to increase after a public health emergency or disaster; those units cannot be used immediately (US General Accounting Office, 2002).

Moreover, the blood supply chain is also influenced by crisis requests because of poor climatic conditions or regular donors postponing donations due to vacation plans. In January 2017 and January 2018, a severe winter blood shortage caused the American Red Cross to issue emergency blood and platelet donation call (American Red Cross, 2018).

Wang and Ma (2015) describe the three blood shortage types: (1) seasonal blood supply shortages due to the decline of blood donors considerably throughout winter and summer seasons, (2) structural blood supply shortages due to the deficient stock of one or more blood groups, and (3) regional blood supply shortages due to blood item overuse in medical-source-concentrated regions. Dealing with blood issues throughout the blood shortage is undoubtedly one of the most challenging blood supply chain management jobs.

- Blood Sharing

Blood sharing of blood shortage is an associate framework for the situation of emergency supply. Through blood sharing, the blood from hospitals with available inventory can be imparted to the received hospitals, which enhances the service level provided by the latter. Since an adequate supply for blood is imperative for good health and medical care services, blood sharing research to solve the blood shortage related issues is very important in health care. The difficulties for blood sharing originate from the inadequate supply, short shelf life, high operating expense, uncertain supply, and high client service level necessity.

The paper (Perera et al., 2009) and poster (Stanger et al., 2011) published and presented by the Blood Stocks Management Scheme (BSMS), a joint venture between the National Blood Service in England and North Wales, has shown that blood sharing can reduce wastage of blood due to expiration and improve blood use efficiency. BSMS has supported sharing stock between hospitals to provide advantages across the blood supply chain. Recent research has also proved that blood sharing can decrease wastage (Yates et al., 2017).

1.5 The Motivation for this Research

In 2004, it was reported that 17% of the collected platelet units within the US were wasted before being transfused (Fontaine et al., 2009; National Blood Centers 2004); and during a survey in 2007, because of blood deficiencies at 1700 US participating hospitals, a total of 492 reportable planned surgeries on at least one day were canceled (Nagurney et al., 2012). Wastage will take place at several points across the blood supply chain. Thus, outdated samples and deficiencies of blood items have remained a problem for hospitals. Given the characteristics of blood and also the pressures in this business, operations research needs to be implemented to help the blood supply chain (Nagurney, 2017). Operations research experts have developed mathematical models in blood inventory management and applied these models to derive procedures and policies (Stanger et al., 2012). Throughout the last couple of years, numerous blood inventory management is established in the area of operations research (Rajendran 2016; Rajendran and Ravindran, 2017, 2019). The following are my motivation for this research:

- The need for better blood inventory management

The value of perishable products within the supply chain declines with time (Blackburn and Scudder, 2009). Blood is not an ordinary commodity. The supply of donor blood is genuinely unpredictable, and the need for blood items is characterized by stochastic behavior. To match supply and demand economically is not easy. A major issue is a way to integrate the current practices in production, inventory storing, and distribution, in addition to thinking about the perishable nature of the products, and to deliver an optimized policy for blood supply chain commodities.

The regional blood center must decide what decisions to make in the operation of blood inventory management and distribution system (Pierskalla, 2005):

- to keep up the best inventory levels for itself
- its inventory distribution policy in heeding to the occasional requests from the Hospital Blood Banks (HBBs) and the Community Blood Centers (CBCs) inventories
- to deliver unused, yet at the same time, valuable blood from an HBB back to be used at other HBBs which have higher request levels and higher use of unused blood before it is expired, and if there is a general blood shortage, the blood center must decide a transshipment policy from some HBBs to others HBBs which have the danger of shortages

The HBB should decide its optimum inventory levels to keep up. These levels, which are independent or in combinations with the CBC, are contingent upon the organization or written agreement between the HBB and the CBC.

Blood inventory management has attracted significant enthusiasm from the Operations Research profession during the last decade or so. By far, the majority of previous research has concentrated on the development of complex inventory models within the blood supply chain management of perishable goods. However, the advanced models proposed in the literature do not seem to be applied in practice (Stanger et al., 2012). Though there has been considerable research on blood inventory management for the blood supply chain, the larger part of the literature centers around one single echelon and does not examine the relationships among the different stages. This could cause a nearsighted perspective of the blood supply chain. Inventory policies and procedures usually do not think about the limitations of supply. Production does not take into account the critical age effect of inventory items (Rajendran and Ravindran, 2017). Those are all examples of issues by only considering single echelons, thus misleading some cases to impractical and unfeasible solutions. The modeling of the complete process operations flow within the blood supply chain is particularly needed. In any event, successfully integrated models for the supply chain would acknowledge the existing constraints within the preceding and succeeding echelons (Osorio, 2015). Further research is needed on modeling blood inventory management considering the entire blood supply chain.

- There is a need for forecasting for blood supply and demand

Hospitals and blood centers face challenging issues for managing blood inventory. Forecasting drives company decisions that the company ought to meet to achieve success. This reality is the same in blood bank management. From the previous discussion, it is known that the uncertainty regarding the need for the various blood products is a key factor in blood bank supply chain management. Adequate forecasting of the amount and timing of future blood demand significantly contributes to the blood inventory control and donor recruiting process. Specifically, decisions regarding the amount of blood products that will be conveyed in inventory, the scheduling of blood collection from donor lists or mobile sites blood collection, and ordering from different blood banks should consider all the factors listed above.

Taiwan blood centers face blood shortage problems due to a lack of accurate forecasting of blood supply. Management of blood supply and demand is regarded as one of the major healthcare supply chain issues. For effective blood supply chain planning, a good forecasting model for blood supply and demand is required.

- There is a need to study blood inventory management under blood demand and supply uncertainty

Inventory management issues are significantly complicated by unknown demand. Solyal et al. (2015), Fortsch and Khapalova (2016), and Rajendran and Ravindran (2017) are some recent researchers that address demand uncertainty issues in inventory management. Previous blood inventory management research generally assumes a known demand or that their demand uncertainties are often modeled as a Poisson or Normal distribution, making it challenging to render significant models in practice. There is a need for inventory management to take the uncertainty of demand and supply into account for the blood supply chain studied.

- There is a need to maintain a sufficient blood inventory to meet regular and emergency blood demand

The emergency blood supply caused by natural and anthropogenic disasters is particularly difficult (Fahimnia et al., 2017). Keeping up a blood inventory that adequately fulfills regular and emergent needs will necessitate additional monitoring and understanding of these patterns (Ellingson et al., 2017). Various cases have demonstrated the necessity for proper blood supply chain methods that facilitate hospitals and medical system support structures to react more efficiently to mass disasters (Gerberding et al., 2007; Williamson and Devine, 2013).

The interest in increased research on blood inventory management in emergency relief operations has gained considerable attention.

- There is a need to study the impact of blood sharing

A cooperative divergent blood supply chain network can be proposed within which every hospital will fulfill its patient demand from its inventory. They may receive an extra quantity of platelet units from alternative collaborating hospitals, which have excess platelets available that day. Thus, the extent of platelet demand fulfillment is increased. This coordinated effort in hospital networking will cut back platelet shortage and outdating.

Blood sharing throughout the blood shortage could be a troublesome issue because it is closely associated with the inventory. There is no comprehensive strategy for blood sharing in current blood inventory management; thus, the goal of this research is to create a new decision-making framework or model, particularly to decrease blood waste in the case of a blood shortage. Most blood inventory management research has improved the situation at the hospital level (Prastacos, 1984). The management of a blood center is far more complicated than that of a hospital. The variety of functions that need to be performed within the blood supply chain structure contribute to its complexity.

This research will examine the blood inventory management with blood centers and hospitals as an entire supply chain, and develop a mathematical model for ordering blood and handling emergencies. This study will also consider the uncertainty factor of blood supply and demand as well as practicable blood sharing.

1.6 Outline of this Thesis

This dissertation starts with an introduction in Chapter 1. Chapter 2 summarizes research areas from previous studies following a detailed review of relevant literature on blood supply chain and inventory management. Chapter 3 proposes forecasting blood supply models. Chapter 4 proposes a Basic Blood Supply Chain Model under supply and demand uncertainty incorporating emergency demand and a case study is presented. Chapter 5 proposes a Blood Supply Chain Model in a divergent blood supply chain under supply and demand uncertainty. Chapter 6 proposes a Multiple Objective Model for Blood Supply Chain inventory management and Chapter 7 concludes the research and provides directions on potential future work.

CHAPTER 2

LITERATURE REVIEW

During the past decades, numerous models have been developed with an emphasis on the different supply chain management areas. The following chapter presents a thorough review of literature on blood product supply chain and inventory management under the following categories:

1. Ordering Policy
2. Forecasting Demand
3. Hierarchy Level
4. Inventory Management
5. Trends in the Type of Approach

2.1 Ordering Policies for Perishable Inventory and Methodology Approach

Inventory ordering management deals with two questions:

- How many units should be ordered?
- At what time should the order be placed?

Modeling of inventory ordering policies is an important topic to discuss in operations research and has made significant progress during the twentieth century. As the perishable products have a limited shelf life coupled with an uncertainty of demand and supply, the inventory ordering models for perishable products pose more complexity and challenges than those of non-perishable ones. One example of a perishable product is blood, and every element of blood has a limited shelf life. Platelets are an important element and have a limited five-day shelf life, RBC has a 42-day shelf life, and plasma and cryoprecipitate have a one-year shelf life (Osorio et al., 2015). The blood supply is somewhat random and the pattern of demand for blood products is most likely a stochastic event (Rajendran and Ravindran, 2017).

Jennings (1973) presented an analytical framework for the entire blood inventory problem considering the individual hospital and regional levels. The effects of various alternative inventory ordering policies on shortage and outdating were analyzed. For an individual, independent hospital blood bank and the relationship between inventory ordering level for outdating and shortage is shown in Figure 2.1, where *s* is designated as daily inventory order level. For example, for an inventory ordering level of 15 units, the shortage is 9%, and the outdating is 8%. This curve represents the trade-off between shortage and outdating.

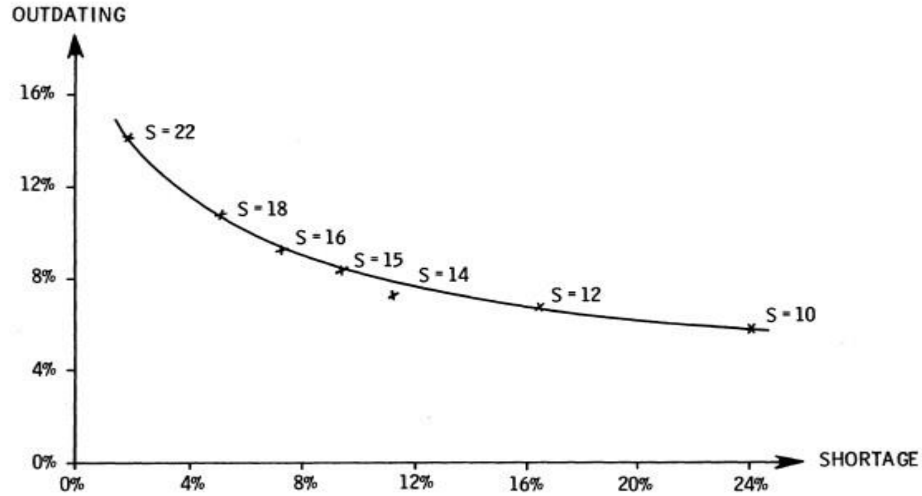


Figure 2.1: Shortage-Outdating Operating Curve by Basic Inventory Policy: an independent hospital: S is designated as daily inventory order level (Jennings, 1973)

At the regional level, the simultaneous effects of the inventory ordering policy on shortage and outdating are shown in Figure 2.2. The potential inventory ordering strategies are affected by the interactions between hospital blood banks. It is concluded that the common inventory system needs to be updated continuously regarding the location of the units, pointing to the need for a large-scale automated information system.

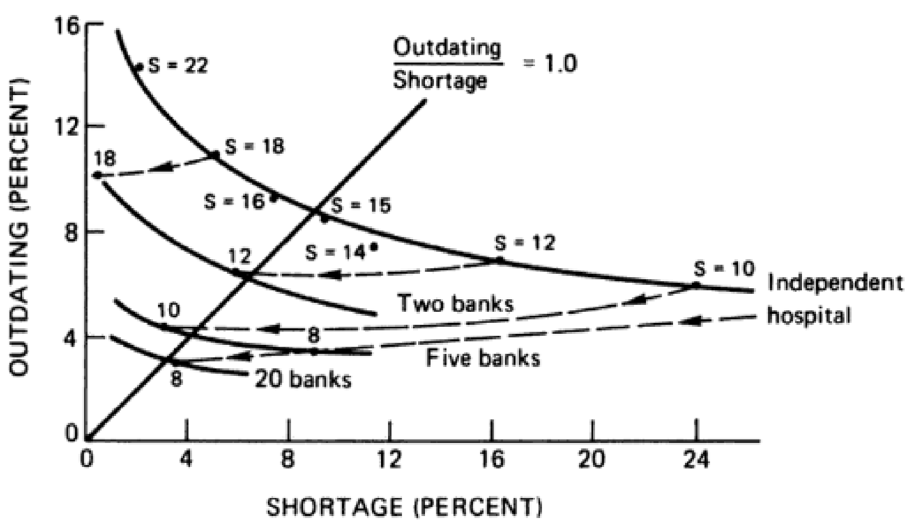


Figure 2.2: Shortage-Outdating Operating Curves for the Threshold Transfer, Common-Inventory Systems (Jennings, 1973)

According to Nahmias (1982) and Pierskalla (2005), there are two blood issuing policies for the hospital: the first-in-first-out (FIFO) policy and the last-in-first-out (LIFO) policy. With the FIFO policy, units of blood that have been in stock the longest are utilized first upon a blood request for patient needs. With LIFO the newest blood units on inventory are issued first upon a request for patient needs. Nahmias and Pierskalla (1973) devised a FIFO policy-based model for the unit that expires in two periods with stochastic demand by minimizing the unsatisfied demand (runouts) costs and deterioration (outdated) costs. Because of the property of cost function structure, it was demonstrated that (s, S) policy is not optimal. The resulting structures are extended to the discounted infinite horizon model, including holding costs and ordering costs. Nahmias (1975) used a dynamic programming method to analyze the optimal ordering policies with a lifetime of exactly m periods, when only runout and outdating costs were charged. When considering perishable goods with a minimal shelf-life, an optimal ordering policy considers the age and time distribution of the inventory assets. Fries (1975) presented the framework and features for the ideal perishable product policy using the lifetime l in a finite-horizon period while the product demand is continuous. One proposition proved that with a maximum shelf life of l, when $n \geq l > 2$, where n is period, neither the 'single critical number' (S) policy nor the 'two-bin' (s, S) policy is optimal for perishable products.

Nahmias (1982) has done a comprehensive review of literature related to the difficulty of determining proper policies for ordering perishable inventory with a fixed life and continuously exponential deteriorating inventory. For fixed-life perishability with stochastic demand, the review is categorized as (1) optimal policies for a single product, (2) approximate optimal policies for a single product, (3) LIFO Inventory, (4) multiproduct and multi-echelon models.

Weiss (1980) studied the (s, S) inventory policy for the case in which it was assumed demand had a Poisson distribution by considering lost sales and backlogs. With the periodic review models, ordering costs, holding cost for items, disposal cost for perished items, and penalty cost for unfulfilled demands are the associated cost. It was determined that a continuous review (s, S) inventory policy is the optimal policy only in the case of linear shortage costs.

Liu and Lian (1999) took a Markov renewal approach to analyze a (s, S) continuous review inventory system with a demand of general renewal process and inventory of immediate stock replenishments. For models with general renewal demand processes, the (s, S) continuous policy can reasonably be optimal.

Tekin et al. (2001) proposed a (Q, r, T) model which indicated that the units are ordered when inventory levels drop below r level or when T units of time have passed since the previous order. Thus, the order policy is not based solely on the current stock supply, but also indirectly on the existing shelf life of the stock as well. This is a periodic review model, where the other models assume continuous reviewing. This policy is noticed to perform better than the regular (Q, r) model.

Haijema (2011) emphasized that Automated Store Orderingsystems and Computer Assisted Ordering systems are using non-perishable policies for ordering. These ordering policies for the systems are dependent on the stock-level alone, not considering the age of goods. Consequently, when applied to perishable products, the expected future outdating of products is not anticipated resulting in unnecessary shortages and outdating.

Zhou et al. (2011) presented a mathematical model to identify optimal inventory policies for platelets using two different replenishment approaches. First, regularly scheduled orders are normally placed at the start of a cycle. Second, upon a supervisor's choice, an extra rush order, featured by an order-up-to level policy could be placed within the cycle. It was proven that the optimum ordering policy could be found, and the optimal cost was greatly affected by the uncertainty of demand, lead times of ordering, seasonality of demand, and information of expedited orders. When demand decreases or demand variance increases, the (s, S) policy becomes more attractive than the (S) policy. Based on the demand information's study and the setting of cost parameters in the hospital, it is suggested that small hospitals should place orders for platelets every other day (particularly hospitals with a high demand uncertainty), and busy hospitals should place orders for platelets every day (particularly hospitals with a low demand uncertainty).

Rajendran (2016) adopted a Mix Integer Programming approach to develop finite and infinite time horizon inventory models to find optimal order quantity and time for platelets for hospitals such that the inventory, wastage, and outdating are reduced.

To address the topic of the classical Economic Order Quantity (EOQ) model, Muriana (2016) presented a mathematical stochastic model including shortage and outdating costs for perishable open-dating (the date when the food was packaged or the last date on which it should be sold or used) foods. This model considered the demand's fluctuations in assuming the demand has a normal distribution and considering the shelf life as a key variable, and thus the most desirable set of parameters was determined, which minimizes the expected total cost.

Pauls-Worm and Hendrix (2018) used a FIFO based policy to compare three different ordering policies over a finite period, perishability, and non-stationary demand: 1) production timing is fixed ahead of time, and an order-up-to stock level is adopted, 2) production timing is set ahead of time with age distribution being considered in the production amount, and 3) the decision on how many units to order depends upon the age distribution of the inventory items. The experimental results of these ordering policies and methods of solution for 81 instances with horizon T with 12 periods were evaluated and an overview was presented. In most cases, the expected total costs resulting from the ordering policies were very close. Depending on the findings from this research, it was important for the management to make decisions on the most appropriate uncertainty strategy and ordering policy.

2.2 Literature Review related to Forecasting Demand for Perishable Products and Methodology Approach

Demand forecasting, particularly for perishable items, is essential for making supply chain decisions such as donor drive scheduling, vehicle routing policies, and inventory management at blood centers and hospitals. Based on historical patient demand data and expert opinions, forecasting models are developed for a finite time horizon. Correct forecasts of the timing and amount of future blood requests have been considered as the key inputs to donor recruiting, decision-making, and inventory control. It is important to gather data of several years for monthly demand forecasting and to recognize seasonality of demand cycles (Pierskalla, 2005). Different types of quantitative models are used to predict future fluctuations of the need for blood. Quantitative models are often in association with past time-series data about blood demand that are originated from a specific repetitive occurrence, for example, variations of monthly blood demand (Filho et al., 2013). Gardner Jr. (1990) studied the effect of the forecasting model on the decisions of inventory policy inside a large physical distribution system. The results demonstrated the vital role that selection of forecasting models plays in determining the investment amount for supporting any target level of client service.

Frankfurter et al. (1974) provided a tool to monitor blood stock levels of 1500 to 1700 blood units based on a short-term computerized model that forecasted blood inventory levels, thus eliminating blood shortages and excessive expirations. Critchfield et al. (1985) explored the potential capabilities of various time series in forecasting the next-day need for platelet. It was found that the time series models are better than simple moving averages models. The prediction of the platelet consumption patterns by a mathematical model application has led to a decreased number of platelets wasted and reduced labor costs for the platelet inventory during the evaluation period.

Pereira (2004) investigated and evaluated three-time series analysis and forecasting models: the autoregressive integrated moving average (ARIMA) model, the Holt-Winters exponential smoothing model, and the neural-network based model for forecasting monthly demand for red blood cell transfusions at one tertiary care. The performance of the forecasting models was evaluated and validated by comparison of the goodness-of-fit statistics, how many months the forecasted supply would have fulfilled forecasted demand of red blood cell (RBC), and the forecasted waste rate of RBC. The results revealed that in one-year, nearly 80% of the time, the ARIMA model or exponential smoothing model generated the RBC demand forecasts, which was inside the ±10% range of the actual RBC demand. Over two years, the exponential smoothing model performed better than the ARIMA model and the neural-network-based method.

Bosnes et al. (2005) used statistical regression techniques for the forecast of blood donor arrivals at the blood bank of Oslo, and found it was valuable in shortening the waiting time for blood donation. The model predicted when the blood donors would arrive, with several factors being used as explanatory variables. It was found that the most important ones among 18 explanatory variables were: donor age, time from making an appointment, arriving at an appointment, contact methods used, total number of donations, donor no-show number, donor arrivals, and delays during the previous two years. Prediction intervals were reduced by 43% by comparison by taking into consideration only the average arrival rate. Schreiber et al. (2005) used statistical regression techniques to evaluate first-year donor frequency, then the likelihood that the donor would return could be predicted using this kind of information. They discovered that those who donated more regularly in the first 12 months were likely to donate again. Motivating current donors to donate regularly during the first 12 months may help the donors establish a regular donation behavior.

Filho et al. (2012, 2013) presented a computerized tool for predicting the blood components' demand. This tool allowed managers to decide how much of the typical weekly demands of platelets and packed red cells should be delivered to hospitals. This tool consists of two models- one is an automation identification model (AIM) and a blood components forecasting (BCF) model. While AIM is based on the Box-Jenkins method (2008) to allow users to evaluate the dataset and identify an adequate parametric model for reliable forecasting, BCF is an application developed to enable managers to deal with the blood components using the time-series forecasting model. Fortsch and Khapalova (2016) introduced several practical methods to predict future demand for blood. Several forecasting models, including the naïve, exponential smoothing (ES), moving average (MA), and time series decomposition (TSD), were tested. They also compared the performance of these methods with an autoregressive moving average (ARMA) model. The results revealed that the ARMA forecasting model performed better for eight out of nine time series models.

Khaldi et al. (2017) explored the capabilities of applying an artificial neural network (ANN) based model to forecast blood demand. The future demand for RBC and plasma were predicted by three ANN-based methods. The data was aggregated into monthly demand after the daily blood demand data was collected from 2010 to 2015. The results revealed that ANN models have greater accuracy in forecasting monthly blood components demand compared to autoregressive integrated moving average (ARIMA) models.

Lestari et al. (2017) used production/operations management and quantitative method software to analyze data by selecting the methods based on the smallest number of errors on forecasting blood components at the blood transfusion station. Four methods of forecasting were used: 1) the moving average (MA) model, 2) the weighted MA model, 3) the exponential smoothing (ES) model, and 4) the exponential smoothing model with a trend. The actual data from the blood transfusion unit was taken and analyzed from January 2015 to December 2015. They found that using the suitable forecasting method can predict the trend pattern represented by the blood components demand. For example, the appropriate forecasting method for whole blood and packed red cells is an exponential smoothing method, rather apheresis is a moving average forecasting method.

2.3 Literature Review related to Blood Supply Chain Hierarchical Level and Methodology Approach

Within the supply chain, there are generally four stages (echelons): collection, production, inventory, and distribution. Several papers contain ‘integrated’ models that include more than one echelon (Osorio, 2015). Jennings (1973) presented the first analytical basis for categorizing the entire blood and blood product inventory problem. This early research presented the issue through hierarchical levels (strategic – tactical – operational) and outlined the effects of various blood inventory policies. Pierskalla et al. (1980) and Osorio (2015) provided an in-depth study and design analysis of the blood supply chain within the United States.

2.3.1 Regarding Hospital level

Brodheim et al. (1976), Katz et al. (1983), and Ledman and Groh (1984) determined a platelet production plan for each weekday to limit platelet outdating while simultaneously maintaining the capability to deliver platelets to meet hospital needs. Vrat and Khan (1976) analyzed the effectiveness of a hospital blood bank system through a simulation model incorporated with a “desired-beginning-inventory-level” policy. It is suggested that the two most important measures of performance for any given blood bank are blood shortage and outdating. Dumas and Rabinowitz (1977) presented new operational policies for reducing blood wastage without adversely affecting shortages in hospital blood banks. Two policies are evaluated using the simulator, one being double-crossmatching, which tests the same unit of blood for compatibility with two potential recipients so that it is available for use by either and ensures that blood is available for both. Another policy is that under certain blood-age conditions and when medically achievable, using Rh-negative blood for Rh-positive patients. The results showed that the wastage was dropped to about 9.8% using single-crossmatching only, the wastage dropped to about 4.4% using double-crossmatching units 14 days or older, and the wastage dropped to 4.2% using double-crossmatching the oldest 25% of the units. While the wastage of Rh negative-to-positive policy was reduced from 19.5% under single-crossmatching to 16.2% using double-crossmatching, it is found that in both positive and negative blood, the most effective reduction in wastage is accomplished by collaborating the double-crossmatching and negative-to-positive policies. Pink et al. (1994) examined the inventory management system of public hospital blood banks located in Sydney to find out what causes the wastage of donated blood. It is recommended that outdating improvements involve changes in inventory management, i.e., changes in crossmatching procedure, understanding blood expiration dates, and effective stock rotation practices. Six months after the recommendations were circulated, the overall outdating was significantly reduced from 5.0% to 0.9%.

Katsaliaki and Brailsford (2007) studied the policies of the blood inventory management system in a representative hospital in the United Kingdom. A discrete-event simulation model was utilized to discover the policies for orders, which would lead to the reduction of blood outdating and blood shortages, improved levels of customer service, improved safety protocols, and cost reduction. The model captured all events that occurred in the blood supply chain, from blood donation to transfusion, and showed how the medium-sized hospital's blood bank could increase customer service and budgetary control. The results of successful policies showed that the total crossmatch release period was reduced to under one day, the transfusion-to-crossmatch ratio was increased to 70%, the RBC holding stock was decreased to four days, 89% (297 units) fewer RBC outdates, an 8% total hospital cost reduction, and 47% (69 units) fewer shortages from the center, etc.

Haijema et al. (2007) conducted a case study on blood bank platelet production and inventory management, which supplies platelets for many hospitals. The Markov Dynamic Programming (MDP) method and the simulation approach were combined to reduce the total cost. This approach was utilized by a Dutch blood bank, with two demand types- 'young' platelets (oncology and hematology) and 'any' age platelets, up to the maximum shelf life (traumatology and general surgery). For a typical week, about 180 platelet pools can be obtained from one blood bank. Approximately 30% of demand was for 'any' age platelets, with 70% for 'young' platelets. It is concluded that the 'nearly optimal' single level (1D) order-up-to and double level (2D) order-up-to policies can be found, where the 1D rule is one level to 'young' platelets, and 2D rule, with one level to 'young' platelets and one to the total inventory. The results showed that the 1D policy performed very satisfactorily, however, the 2D policy performed to an almost optimal level.

Heddle et al. (2009) analyzed product inventory/disposition data of red blood cells (RBC) at 156 hospitals for 21 months and used logistic regression techniques to ascertain what elements (month, distance to blood provider, monthly blood transfusion activity, type of hospital, and rural district) would affect RBC outdating. RBC outdating was considerably impacted by three factors: blood provider distance, average monthly blood transfusion activity, and month. Based on the factors that affected wastage, a technique is built to classify the hospitals into groupings. Each group would then be able to set up a reference target. Group 1 consisted of 73 hospitals with an RBC target wastage level of 0.4%, Group 2 consisted of 59 hospitals with a target wastage level of 1.1%, and Group 3, comprised of 24 hospitals with a target wastage level of 20.3%.

Gunpinar and Centeno (2015) introduced a stochastic integer programming model within a planning horizon to reduce the shortage and wastage levels of platelet components and RBC at a hospital. The models take into account blood unit age for units stored in stock, the demands for two patient types, demand rate uncertainty, and the ratio of crossmatch-to-transfusion. The results showed that the average wastage rate decreased from 19.9% to 2.57%. Shortages and total costs were reduced by 91.43% and 20.7%, respectively. This model would help determine suitable order sizes to reduce the shortage and wastage costs as well as the total costs.

Attari et al. (2017) released a goal programming model to diminish wastes and shortages of blood components in hospitals. Demand and supply data were collected from 35 various hospitals and clinical centers located in Tabriz, Iran, and solved by the model under 3 different scenarios and 18 time periods. Computational results demonstrated that hospitals' holding, transportation, and waste costs compared to their shortage costs are very low. Hospitals tend to accept blood products' holding and waste costs to fulfill the demands of patients who receive blood products.

2.3.2 Regarding Blood Center Level

Frankfurter et al. (1974) introduced a computerized blood inventory forecast system to manage inventory levels at an Albany, New York regional blood collection and distribution center system. Total blood collections amount to approximately 65,000 units annually, and about a two-week supply of blood is in inventory (available) in the region at any period of time. This inventory level projection model is used to alert regional blood center management when potentially low or high blood inventory levels occurred. Therefore, when inadequate inventory levels were forecasted during a period, preventive action will be taken immediately by either increasing or reducing collections of blood. Cumming et al. (1976) established a strategic planning model for a blood supply region. The goal of this model is to assist the blood provider of the region to mitigate seasonal differences in blood demand and supply. A Markovian population model is applied to forecast various performance measures for a blood supply region. The model needs past performance of bloodmobile sponsors, quotas, and forecasts of demand. An improvement in the blood collection and scheduling operations could be made by implementing the strategic planning model; for example, scheduling is improved by changing the dates for only 25 of the 300 blood collections planned by the supplier.

Prastacos (1978) analyzed the distribution policies of a perishable good which was allocated from a central location to various regional location, namely, the rotation policy where the unused and not outdated product was returned to the center, and the retention policy, where to return the unused product to the center are not possible. It is shown that the optimal myopic rule reduces shortage and outdating expenses for a given period and is straightforward to apply in a practical setting.

Prastacos and Brodheim (1980) described a FIFO policy-based decision support system, the 'Programmed Blood Distribution System (PBDS)', which is for regional blood administration. There are three features of the system: (1) a centralized management of blood bank, instead of by individual hospitals, (2) deliveries by prescheduling, and (3) a distribution system based on blood that is "rotated" between hospitals. The region's blood distribution system performance has also been greatly impacted by the PBDS. Before its implementation, an estimated 20% of their blood resources were outdated, and on average, they received 7.8 deliveries a week per hospital, which were all unscheduled. Once PBDS was implemented, the region's blood outdating was decreased to roughly 4%, and the weekly deliveries were decreased to approximately 4.2 deliveries per hospital. Of these deliveries, only 1.4 were not scheduled beforehand. PBDS has been implemented and is currently operational in 38 hospitals in Long Island, New York.

Denesiuk et al. (2006) developed a red blood cell unit redistribution system for outdated units. The main idea of this system is to transfer the nearly outdated RBC units from a low utilization of blood hospitals to a high utilization of blood hospitals. It was found that the redistribution systems can be a successful practice to decrease the wastage rates of RBC units, thus increasing overall available inventory levels in the blood system. Four remote sites located in northern Alberta, Canada, implemented this redistribution program. The first year the blood redistribution system was implemented, the on-site number of discarded RBC units was decreased in all four sites. Between April 1, 2003, and March 31, 2005, 106 RBC units were effectively transferred from low-usage sites to high-usage sites.

2.3.3 Regarding Supply Chain level

Kendall (1980) recommended a good model for solving planning problems with multiple objectives. In his paper, four major objectives were identified for a regional blood collection and distribution system: (1) to reduce costs associated with donor recruitment and collecting and processing of blood; (2) to minimize blood shortages at participating hospital blood banks; (3) to diminish wastages of blood; and (4) to reduce transfused blood age. This model used two approaches, sequential elimination by a combination of constraints and a trade-off method to select the most useful combination of goals.

Rytilä and Spens (2006) constructed a simulation model to be used for increasing the effectiveness of blood supply systems in Finland. The goals of their research were to reduce total, outdating, and backorder costs, and maintain the current level of blood accessibility. Detailed data was gathered and validated. The results of the simulation experiments suggested that simulation modeling approaches provided a very useful tool for risk and uncertainty management in healthcare supply chains. Kopach et al. (2008) anticipated the demand according to FIFO policy and proposed a queuing model based on the key concept-inventory systems of perishable commodities and the level that crossing techniques that were used to determine an optimal policy to keep up the balances between emergency and discretionary demand, customer service, costs, and minimizing shortages and outdating at the blood center. Data was gathered by blood type and included red blood cell units delivered from regional blood centers. Compared with current control techniques by using simulation, this model is shown to be effective using real data acquired from Canadian blood services.

Katsaliaki (2008) studied the entire UK supply chain for blood and took a discrete event simulation model to examine and identify good ordering, inventory and distribution practices for the supply chain. All the acquired data was gathered from the National Blood Service Center in Southampton, along with the hospitals served by the blood center. The study's purpose was to find policies that produced better and more cost-effective supply chain management. The results from successful policies showed that the total crossmatch release period was reduced to under one and half days, the ratio of the transfusion-to-crossmatch was increased to 70%, and the average of RBC stock was held approximately four days, etc.

Ghandforoush and Sen (2010) presented a typical model of the Decision Support System (DSS) for bloodmobile scheduling and platelet production for a regional blood center. The goal was to lessen the costs of blood collection, production, and shortages. One vital DSS aspect is an equipped non-convex integer optimization model that assisted the regional blood center with scheduling whole blood transportation from collection stations to the regional processing center. In the trial, the predetermined weekly component schedule is established off of daily production of 350 to 475 platelet units, with the production varying based on the day of the week. Historical data was used to establish daily demand, with the addition of safety stock to cover estimation error. Results from this test suggested that by implementing an improved production strategy and mobile assignment plan, the proposed DSS could do superior to meet the daily demands.

Dillon et al. (2017) suggested a two-stage stochastic programming model to determine superior policies for periodic review of RBC inventory management. The model's goal is to decrease operating costs, blood shortage, and outdating as much as possible, while considering the perishability and demand uncertainty. To assess the performance of the proposed framework, a case study was used. The case study collected realistic data to represent daily blood demand determined from the average and the standard deviation of the demand for eight types of blood. The model proposed could easily be adapted for the consideration of different planning horizons periods, various lead times, and blood products with limited shelf lives such as plasma and platelets. Moreover, it was shown that blood inventory management could achieve additional increases in performance by considering blood substitutions.

2.4 Literature Review related to Inventory Management and Methodology Approach

Blood Inventory Management has attracted huge interest from the operations research profession during the last decades (Ekici, 2017). Prastacos (1984) presented an exhaustive literature review on blood inventory management. The majority of the literature has concentrated on inventory management, specifically focusing on blood product perishability (Pierskalla, 2005). There are other papers that concern inventory management, including studies about demand forecasting, emergency blood demand plans, best practices, computerized information management systems, the extensions of blood component shelf life, and additional issues related directly or indirectly to the supply chain management of blood. It is suggested that novel research will focus on the development of new inventory policies as opposed to adopting classic inventory models such as min-max inventory models or fixed order interval policies for blood products.

2.4.1 Blood Inventory Management for Inbound Problems

Inbound problems include ordering policy, issuing policies, inventory allocation, crossmatching policies, planning for collections, and other issues that related directly or indirectly to blood supply chain management (Beliën and Forcé, 2012).

Jennings (1973), Prastacos (1984), Sirelson and Brodheim (1991), Pierskalla (2005), Haijema et al. (2009), and Van Dijk et al. (2009) have presented fixed order interval inventory models that exhibited platelet inventory management effectiveness at specific blood centers and hospitals.

Federgruen et al. (1986) studied a distribution routing inventory model for perishable items that were allocated from a regional center to various regional sites with indiscriminate needs. The study’s goal is to minimize transportation, shortage, and outdating costs. This study analyzed two delivery methods: method one assumed all demand points receive individual deliveries; and method two chose a fleet of vehicles to travel multiple-stop routes to make combined deliveries. The per-unit costs among locations were different and the issues of allocation and distribution/routing were examined together. Computational results showed that the traveling costs are considerably reduced by using the joint methods, but a very small drop in inventory performance was seen as well.

Jagannathan and Sen (1991) focused on the storing of crossmatched blood, and they developed a model to resolve the outdates and shortages of crossmatched blood. It selected inventory parameters that were generally accepted, such as a proportion of transfused, crosshatched blood, and the range of days when that crosshatched blood is discharged. This provided the administrator of the blood bank with a tool for deciding desired free (or unallocated) inventory levels that would reduce operating costs and improve services.

Michaels et al. (1993) used a simulation model to assess several scheduling approaches for blood donor arrival to a Red Cross blood drive. In the Greater Chesapeake and Potomac Blood Services Region, registration, health history, and venipuncture service time data was gathered. The results of the experiments recommend that a fully-scheduled system should be employed for blood drives. This includes all donors being scheduled beforehand without slots intentionally left open for walk-ins. After all possible donors have signed up, any available slots can be filled by walk-in donors.

Abbasi and Hosseinifard (2014) examined different issuing policies for a limited lifespan inventory system with unmanageable replenishment and a modified FIFO policy was presented. Their adapted FIFO policy separates inventory into two parts. Part one holds items under an age threshold and applies the FIFO policy in each part and the LIFO policy between the parts. Several cases used in their analysis showed the modified FIFO policy outperforming the FIFO and LIFO policies, where a single economic function or formulated as a multi-objective model was defined as the objective function.

Duan and Liao (2014) introduced a new simulation optimization (SO) structure for inventory management in the blood supply chain with A, B, AB, or O(ABO) blood group compatibility. A study was presented and accomplished optimizing the red blood cell order-up-to guidelines for a single-hospital single-blood center supply chain system by considering the products of eight different blood groups and their suitable replacements. An ideal solution was identified for all three situations, and the prospective cost savings provided by compatible substitution was measured by the proposed SO framework. Allowing ABO/Rh (D)-compatible blood substitution helped decrease outdating by at least 16% throughout the system, even under the most restrictive maximal shelf life. For a shelf life of 14 days and 21 days, the highest outdating rate was kept as low as 2% by the proposed framework.

Najafi et al. (2017) took the blood demand and supply uncertainty and possible blood transshipment into consideration and then proposed a blood inventory management model for managing, ordering, and issuing to minimize blood shortage and outdating. This model also considered possible substitutions among different blood types in the blood transfusion process. The results of a numerical experiment demonstrated that within the planning horizon period, blood outdating in the hospital was decreased by using a lesser transshipment value threshold. A higher crossmatch to transfusion (C/T) ratio value showed an additional decrease in blood shortage and wastage.

During emergencies and disasters, extra blood is necessary. According to Butch (1985), an emergency is one of the internal factors that influence blood bank inventory management. Boppana and Chalasani (2007) developed a continuous-time Markov chain model to establish the ideal rate of blood acquisition in emergencies to minimize the amount of blood collection. This Markov model highlights how to tradeoff acquisition rates and maximize blood product storage for a certain level of availability. In the paper by Erickson et al. (2008), it is reported that the Yale-New Haven hospital blood bank has implemented an emergency blood management plan, including upkeep of a reserve frozen blood supply. This supply is not intended to fulfill the enormous transfusion need accompanying extreme or sustained disasters. Instead, it serves as a short-term stock until blood center support is restored. Zhou et al. (2009) analyzed a periodic review inventory system for limited lifespan products under two replenishment modes that include routine orders issued at the start of a cycle and the manager placed and emergency orders within the cycle. It is proven that when an ideal order-up-to level policy is used, expected costs are minimized. The numerical results showed that the total anticipated cost is reactive to the normal order policy. The optimal policy is reactive to changes in the anticipated demand.

2.4.2 Blood Inventory Management for Outbound Problems

Outbound problems consider issues related to supply and distribution scheduling (Beliën and Forcé 2012).

Prastacos (1978, 1981); Gregor et al. (1982); Sapountzis (1984); Denesiuk et al. (2006) focused on models for distributing blood from a regional blood center to different hospitals with consideration of outdating and shortages. To thoroughly understand what defines the efficiency of a blood inventory, Pereira (2005) used a stochastic model to simulate the regular processes over a few days in inventory management in a hospital blood bank. The outdating and shortage rates grew exponentially with a coefficient of variation (CVAR) in daily transfusion, and increasing the remaining shelf life (RSL) could partially counterbalance this effect. For hospitals not holding crosshatched inventories, the coefficient of variation (CVAR) in daily transfusion is the major parameter for identifying the performance of blood inventory management. In a daily transfusion, hospitals with a large CVAR need young red blood cell (RBC) units, however, hospitals with smaller CVAR perform well with older units.

Hemmelmayr et al. (2009) investigated the Austrian Red Cross blood product delivery strategies. They used an Integer Programming and variable neighborhood search approach to examine the benefits of substituting in vendor management, with a deterministic usage rate, for current vendee management of inventory. The computational study showed that a cost was reduced by approximately 30%. Otherwise, the variance was comparatively small (averaging less than 5%) between the two proposed delivery approaches. In situations with tight constraints (i.e., hospital with restricted space for storage and minimal spoilage periods), concentrating on optimizing delivery day decisions results in marginally improved outcomes, while in a less constrained situation, concentrating on consistent delivery patterns provides marginally improved outcomes. Because of the uncertainty with medical usage rates, Hemmelmayr et al. (2010) extended this method to deal with stochastic product usage. A technology for the development of delivery routes for the blood product supply to hospitals was developed. The technology takes into account fluctuations in blood product usage at hospitals and is sampling-based. A range of emergency delivery options is also taken into consideration.

Pierskalla (2005) demonstrated time series methods to forecast the mean daily blood requests for inventory control. In the methods, simulation model and statistical analysis were utilized to build up a target inventory decision function for inventory levels at an independent hospital blood bank, at a centralized hospital blood bank system (HBBs), and community blood centers (CBCs).

Wang and Ma (2015) presented an inventory infrastructure for both main delivery and affected blood banks during emergency blood shortages. A transshipment model is developed for shipping blood units. Two product selection approaches were compared: age-based and quantity-based policy. The simulation experiments showed that under first-in-first-transship (FIFT) methods, the total number of expired units was lower when using the age-based policy when comparing with the quantity-based policy. The expiration rate of all systems is within the normal range.

2.5 Literature Review related to Trends in the Type of Approach

Problems of supply chain management related to blood products have been modeled utilizing a variety of methodologies and approaches. Especially, the most well-known solution methods presented in the literature are simulation methodology, mixed integer programming, goal programming, dynamic programming, and multiple objectives approaches. The real-world problems are analyzed and solved by utilizing each approach alone or together with other methods (Gunpinar, 2013).

Numerous research papers on the blood supply chain started being fully deterministic, and over the years expanded to deal with the stochastic setting (Beliën and Forcé, 2012). The publications including a stochastic setting have exceeded the number of those including a deterministic setting. Within the past 10 years, the disparity has just turned out to be larger. This implies that research in the future will keep concentrating on a stochastic (uncertainty) setting.

A summary of this literature reviews is presented in Table 2.1:

Table 2.1: Summary of Literature Reviews

Article	**Type of problem**	**Objective**	**Hierarchical Level**	**Methodology**
Jennings (1973)	Inbound and Outbound	Minimize cost function which includes two cost components- shortages and outdating	Hospital	Mathematical stochastic model
Frankfurter et al. (1974)	Inbound and Outbound	Forecast transfusions and alert short-term inventory level of blood supplies	Blood center	Exponential smoothing techniques
Nahmias (1975)	Inbound	Minimize cost function which includes four cost components- ordering, holding, shortages, and outdating	Irrelevant	Dynamic programming
Fries (1975)	Inbound	Minimize cost function which includes four main components- ordering, holding, procurement, and wastage costs, in addition to a discounting factor	Irrelevant	Markovian model and dynamic programming
Brodheim et al. (1976)	Inbound	Minimize shortage rates to determine what inventory levels should set for hospital blood banks	Hospital	Statistical models
Cumming et al. (1976)	Inbound	Minimize the seasonal variance between supply and demand of blood to improve scheduling of blood collection	Blood Center	Markovian population model
Vrat and Khan (1976)	Inbound	Suggest an optimal inventory policy for a hospital blood bank to minimize the total shortage and outdating	Hospital	Simulation model

Prastacos (1978)	Inbound	Derived optimal myopic rules to minimize both shortage and outdating costs for one period	Blood center	Demand distribution model
Gardner Jr (1979)	Irrelevant	Compare multiple regression forecasting model vs Box-Jenkins models	Hospital	Multiple regression forecasting model
Prastacos and Brodheim (1980)	Inbound and Outbound	Minimize expected outdating and shortage costs and maximize distribution of regional blood resources while meeting policy constraints	Blood center	Simulation model
Kendall (1980)	Inbound and Outbound	Minimize shortages, outdating, age of blood transfused, and regional operating costs	Blood center	Integer Programming
Weiss (1980)	Outbound	Minimize expected average cost which includes four cost components – ordering, holding, disposal, and penalty	Irrelevant	Mathematical proofs and optimal derivations
Prastacos (1981)	Inbound and Outbound	Reduce the expected shortages and outdates in the area to find good allocation policy	Blood center	Metaheuristics, Mathematical proofs and optimal derivations
Federgruen et al. (1986)	Inbound and Outbound	Minimize cost function which includes three components- shortage cost, outdating cost, and transportation cost	Blood center	Integer Programming
Michaels et al. (1993)	Inbound	Evaluate several effective approaches for the blood donors arrivals scheduling to a Red Cross blood drive	Blood center	Simulation Model

Lian and Liu (1999)	Inbound	Minimize cost function of four cost components- ordering, holding, shortage, and outdating to compute optimal parameters s^* and S^*	Irrelevant	Markov renewal approach and mathematical derivations
Tekin (2001)	Inbound	Minimize the expected total cost of three components- ordering cost, holding cost, and outdating cost under the service level constraint	Irrelevant	Markov approach and Mathematical derivations for optimal ordering policy
Pereira (2004)	Inbound	Compare three time-series methods	Hospital	Time-series methods
Bosnes et al. (2005)	Inbound	Predict blood donor arrival to allow for improved donation planning	Blood center	Statistical analysis
Schreiber et al. (2005)	Inbound	Examine whether first-time donors with recurrent donations in the first year were more likely to become consistent donors	Blood center	Logistic regression techniques
Boppana and Chalasani (2007)	Inbound and Outbound	Establish the ideal procurement rate of blood during emergencies	Supply Chain	Markov chain model
Kopach (2008)	Inbound	Examine trade-offs between multiple demand levels, service levels, operating costs, and also minimizing shortages and wastage	Blood Center	Stochastic queuing model and level crossing techniques using simulation
Hemmelmayr et al. (2009)	Outbound	Generate and assess two alternative delivery strategies by minimizing the number of deliveries	Blood Center	Integer programming, Variable neighborhood search

Van Dijk et al. (2009)	Inbound	Identify an ideal production policy to minimize outdating cost and shortages cost	Hospital and Blood Center	Stochastic dynamic programming with simulation
Ghandforoush and Sen (2010)	Inbound	Reduce the total system daily costs which include transportation costs, production costs, and the cost due to the loss of platelets	Blood Center	Non-convex integer optimization model, Mathematical proofs and derivations
Zhou et al. (2011)	Inbound	Minimize expected total cost including ordering, shortage, and outdating cost, to analyze a periodic review inventory system for a perishable product under two replenishment modes	Hospital	Dynamic programming
Filhoet al. (2012)	Inbound	Forecasting blood components demands	Hospital	Computerized Seasonal Autoregressive Integrated Moving Average (SARIMA) models
Filhoet al. (2013)	Inbound	Forecasting blood components demands	Hospital	Computerized Box-Jenkins Seasonal Autoregressive Integrated Moving Average (BJ-SARIMA) models

Duan and Liao (2014)	Inbound	Minimize the expected system-wide outdated rate under a predetermined maximally allowable shortage level	Hospital and Blood center	Simulation optimization (SO) framework incorporated with a new metaheuristic optimization algorithm
Gunpinar and Centeno (2015)	Inbound	Minimize the total cost which includes shortage, outdating, purchasing, and holding costs at a hospital within a planning horizon.	Hospital	Stochastic integer programming
Wang and Ma (2015)	Outbound	Develop an age-based transshipment model to minimize the sum of weight coefficients of the selected transshipping products	Hospital	Mixed integer programming and simulation
Fortsch and Khapalova (2016)	Inbound	Accurate blood demand forecasting to lower wastage and excess inventory	Blood Center	Box–Jenkins methodology
Muriana (2016)	Inbound	Minimize the expected total cost- shortage, outdating, and holding costs	Irrelevant	Mathematical stochastic model and differential equation with closed form solution
Rajendran (2016)	Inbound	Minimize the expected total cost- ordering, purchasing, shortage, outdating, and holding costs	Hospital	Mix integer programming
Attari et al (2017)	Inbound	Minimize shortage cost and wastage cost of blood products	Hospital	Multi-choice goal programming
Dillon et al (2017)	Inbound	Minimize operational costs, blood shortage cost, and outdating cost	Blood supply chain	Stochastic programming

Khaldi et al. (2017)	Inbound	Forecasting monthly demand of three blood components- red blood cells (RBC), plasma (CP) and platelets (PFC)	Blood Center	Artificial Neural Networks (ANNs)
Najafi et al. (2017)	Inbound	Manage blood ordering and issuing to minimize blood shortage and wastage	Hospital	Multi-objective integer programming and chance constraint programming
Lestari et al. (2017)	Inbound	Select best method for forecasting blood transfusion unit	Supply Chain	Production/Operations Management, Quantitative Method (POM-QM) software
Pauls-Worm and Hendrix (2018)	Inbound	Minimize the expected total cost containing production, shortage, and outdating costs	Irrelevant	Stochastic programming model with a chance
Proposed Research	**Inbound and Outbound**	**Minimize the expected total cost including ordering, purchasing, shortage, outdating, and transportation costs**	**Blood supply chain**	**Mixed Integer Programming, Stochastic Programming, Goal Programming**

A summary of objectives in this literature reviews is presented in Table 2.2:

Table 2.2: Summary of Objectives in Literature Reviews

Article	**Objective**					
	Ordering	**Purchasing**	**Shortage**	**Outdating**	**Holding**	**Transportation Cost**
Jennings (1973)			√	√		
Nahmias (1975)	√		√	√	√	
Fries (1975)	√	√		√	√	
Brodheim et al. (1976)			√			

Vrat and Khan (1976)			√	√		
Prastacos (1978)			√	√		
Prastacos and Brodheim (1980)			√	√		
Kendall (1980)		√	√	√		
Weiss (1980)	√		√	√	√	
Prastacos (1981)			√	√		
Federgruen et al. (1986)			√	√		√
Lian and Liu (1999)	√		√	√	√	
Tekin (2001)	√			√	√	
Van Dijk et al. (2009)			√	√		
Ghandforoush and Sen (2010)		√		√		√
Zhou et al. (2011)	√		√	√		
Gunpinar and Centeno (2015)		√	√	√	√	
Muriana (2016)			√	√	√	
Rajendran (2016)	√	√	√	√	√	
Attari et al. (2017)			√	√		
Dillon et al. (2017)		√	√	√		
Najafi et al. (2017)			√	√		
Pauls-Worm and Hendrix (2018)		√	√	√		
Proposed Research	√	√	√	√	√	√

2.6 Research Goals on Blood Inventory Management

Blood supply chain management requires that both hospitals and blood centers be increasingly innovative and cost-effective in collecting, producing, and delivering blood products and services (Ghandforoush and Sen, 2010; Belien and Force, 2012). An appropriate approach should be taken to deal with inventory costs, blood platelet ages, short-shelf life of blood platelets, and consideration of demand and supply uncertainties. This research is an endeavor toward that direction. The primary goal of this research is to propose a few blood inventory management models for the blood supply chain while aiming for the subsequent research goals:

- **More reliable Forecasting for Blood Supply and Demand**

Forecasting drives company decisions in the number of demands that the company ought to meet to achieve success. From the previous discussion, it is known that the uncertainty about the need for the various blood products is a major factor in blood supply chain management. Thus, the accuracy of forecasts on the amount and timing of future blood demand significantly contributes to blood inventory control and the donor recruiting process.

Taiwan blood centers face blood shortage problems due to a lack of accurate forecasting of blood supply and demand (Taiwan Blood Services Foundation Statistics, 2017). A good forecasting model for blood supply and demand is required for the successful planning of a blood supply chain.

The proposed research considers developing forecasting models using predictive machine learning analytic tools. These analytic techniques are important in growing industry applications of machine learning.

- **Better Blood Inventory Management**

Given the characteristics of blood, operations research can give help with blood supply chains (Blake, 2009; Nagurney, 2017). Research related to blood inventory management is dominated by operations research experts who build mathematical models and apply them to develop policies (Stanger et al., 2012). Nevertheless, in 2004, it is reported that 17% of platelet units gathered within the US became out-of-date before the units were used (National Blood Centers, 2004; Fontaine et al., 2009); and a total of 492 reportable elective surgeries cancellations on at least one day were because of blood deficiencies at 1700 US hospitals, taken from a 2007 survey study (Nagurney et al., 2012). Thus, outdated and deficiencies of blood items have been and still is a problem for hospitals. There is a need for better blood inventory management.

Although research of blood inventory management for the blood supply chain exists, not many cases of integrated models of supply chain and consideration of multiple features have been considered. Most of the literature centers on single echelons. This could mislead some cases into unpractical and unfeasible solutions. A need exists for modeling the whole process flow within the blood supply chain. In any event, integrated models would acknowledge constraints within the front and back stages (Osorio, 2015). Blood inventory management is a trade-off, guaranteeing 100% accessibility to all blood products in the least time while minimizing wastage. The proposed research considers developing models in blood inventory management for the entire blood supply chain to make good management planning decisions, such as when to collect blood from donors, how many units to collect, proper assignment of manpower for collecting blood in donor drives, blood component testing process, etc.

- **Incorporate Blood Inventory Management with Blood Demand and Supply Uncertainty**

Minimizing blood wastage and shortages poses a major challenge in blood management at hospitals and blood centers. On account of demand and supply uncertainty, mitigation efforts to manage and minimize the impact of outdated blood and shortages represent a challenging problem for hospitals (Najafi et al., 2017). Solyal et al. (2015), Fortsch and Khapalova (2016), and Rajendran and Ravindran (2017) are the latest researchers to address the challenge in inventory management of demand uncertainty. The previous investigation on blood inventory management assumed demand was known, or their uncertainties are often modeled as a Poisson or Normal distribution, making it difficult to render significant models in practice. The proposed research considers developing models in blood inventory management, considering the whole blood supply chain under the uncertainty of blood supply and demand.

- **Effective Blood Inventory Management to meet Emergency Blood Demand**

Keeping up blood inventories adequately to fulfill the routine and emergent loads, will require additional monitoring and understanding of these patterns (Ellingson et al., 2017). Various cases demonstrate the necessity for blood supply chain solutions that allow hospitals and medical system infrastructures to react successfully to mass casualty events (Gerberding et al., 2007; Kamp et al., 2010; Williamson and Devine, 2013).

Also, blood can be sent back to the blood center due to false-negative bacterial contamination or when extra units are ordered. In these cases, the reverse shipment cost has to be considered in the model. No previous research has been found that has taken into account the reverse shipment cost and the associated changes in stock inventory. This research will consider the area of emergency relief operations and collaboration with closed-loop blood supply chains as well.

- **Blood Sharing in Blood Supply Inventory Management**

The issues with blood sharing come from the inadequate supply, finite shelf life, high operating expense, uncertainty of demand and supply, and the requirement for a high level of customer service (Wang and Ma, 2015). Through a divergent blood supply chain network, the blood inventory of the delivery hospital can be imparted to affected hospitals, which enhances their service levels. Gregor et al. (1982) employed a simulation model to evaluate the costs and effects of several different operational policies for a regional blood center. It was found that lower expiration and shortage rates were yielded from a periodic redistribution of the regional inventory.

Blood sharing throughout the blood shortage could be a troublesome issue because it is closely associated with the inventory. In current practice, there is still no broad approach for blood sharing; thus, this research will surely aim to create a new decision-making structure, particularly for reducing blood waste during blood shortages.

Overall, this research will examine blood inventory management in blood centers and hospitals as an entire supply chain, and develop a mathematical model with the goal of managing blood ordering, blood sharing, emergency demand, and inventory. This study will consider blood supply, demand uncertainties, and blood sharing feasibility. At last, numerical experiments will be devised to show the model's outcome and assess the impact of various parameter settings for blood inventory management.

CHAPTER 3

BLOOD SUPPLY FORECASTING

In managing blood inventory, the demand for different blood products is a primary source of uncertainty within the management of the blood supply chain. Correct forecasts of the quantity and timing of future blood requests have been the important input of data to inventory control and donor recruiting decision making (Pierskalla, 2005). Lestari et al. (2017) indicated that the forecasting could predict the data trend observed and future demand for blood components. This chapter will be using the historical data of Taiwan's blood center and select the best forecasting methods to predict future blood supply and demand. Figure 3.1 represents the blood operation process in Taiwan's blood centers.

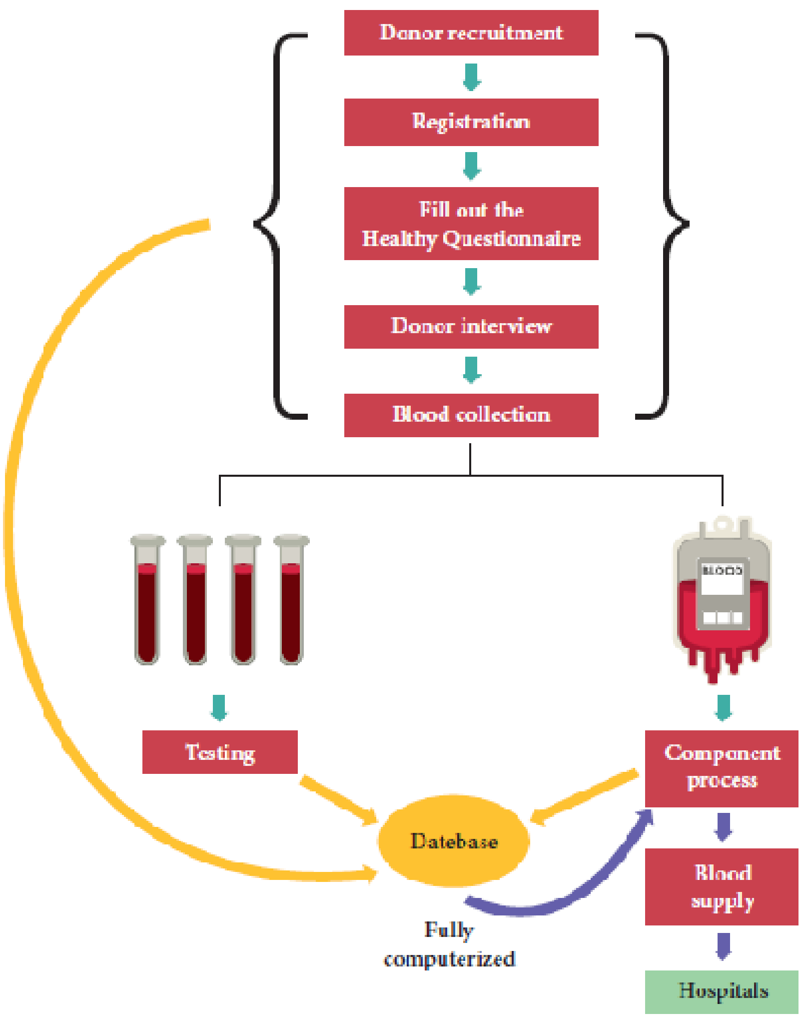


Figure 3.1: Blood Operation Process (Taiwan Blood Service Foundation, 2019)

Based on the literature review on forecasting demand for perishable products described in chapter 2, it is concluded that the best performance forecasting models are: autoregressive moving average (ARMA) method, autoregressive integrated moving average (ARIMA) method, exponential smoothing model (ESM), and machine learning artificial neural network (ANN) based approach.

3.1 Time Series Forecasting Methodologies

This section discusses the seven time series forecasting methods used in this case study.

3.1.1 Autoregressive (AUTOREG) Model (Nahmias, 2015; SAS, 2017)

The AUTOREG procedure estimates and forecasts linear regression models for time series data when the errors are auto-correlated or heteroscedastic. The autoregressive model regresses the value of the series at time t (Y_t) on the values at times $t-1, t-2, \ldots, t-p,$ the mathematical formula is expressed as given in Equation (3.1).

$$Y_t = \alpha_0 + \alpha_1 Y_{t-1} + \alpha_2 Y_{t-2} + \cdots + \alpha_p Y_{t-p} + \epsilon_t \tag{3.1}$$

Where $\alpha_0, \alpha_1, \alpha_2, \ldots, \alpha_p$ are the linear regression coefficients, Y_t is the value at time t and ϵ_t is the random error variable and is generally assumed to have a normal distribution with mean 0 and variance σ^2 (i.e., normal $(0, \sigma^2)$).

3.1.2 Autoregressive Moving Average (ARMA) Models (Pankratz, 1983; Nahmias, 2015; SAS, 2017)

ARMA model is one of the basic tools in time series modeling. Suppose the time series $Y_1, Y_2, \ldots., Y_t$ is stationary stochastic process time series, the expression ARMA (*p*, *q*) represents the model with autoregressive order of p and moving-average order of q. This model is a combination of the AR (*p*) and MA (*q*) models, where AR (*p*) is written as $Y_t = a + \emptyset_1 Y_{t-1} + \emptyset_2 Y_{t-2} + \cdots + \emptyset_p Y_{t-p} + \epsilon_t$ and MA (q) is written as $Y_t = b - \theta_1 \epsilon_{t-1} - \theta_2 \epsilon_{t-2} - \cdots - \theta_q \epsilon_{t-q} + \epsilon_t$.

Y_t is the observation value at time t. The ARMA (*p*, *q*) process is generally written in the form given in Equation (3.2).

$$Y_t = c + \sum_{i=1}^{p} \emptyset_i Y_{t-i} - \sum_{i=1}^{q} \theta_i \epsilon_{t-i} + \epsilon_t \tag{3.2}$$

Where a, b, c are constants, ϵ_t is the random error variable and is generally assumed to have a normal distribution with mean 0 and variance σ^2; $\emptyset_1, \emptyset_{2,} \ldots, \emptyset_p$ are the autoregressive coefficients to be estimated, and $\theta_1, \theta_{2,} \ldots, \theta_q$ are the moving average coefficients to be estimated.

3.1.3 Autoregressive Integrated Moving Average (ARIMA) Model (Pankratz, 1983; Nahmias, 2015; SAS, 2017)

The ARIMA (autoregressive integrated moving average) approach was made popular by Box-Jenkins models (Box et al. 2008). The ARIMA procedure is functioning as a linear combination of its current values, past values, past errors, and past values of other time series (predictor time series) to predict a future response value in a time series.

With time series nonstationary behavior, the above ARMA (p, q) model can be extended and written using difference which is defined as: $Y_t - Y_{t-1} = (1 - B)Y_t = \nabla Y_t$

Where t is the index of time; Y_t is time series $\{Y_t: 1 \leq t \leq n\}$ at time t; B is the backward shift operator, which means that B has the effect of shifting the data back one period (i.e., $BY_t = Y_{t-1}$).

3.1.4 Seasonal ARIMA Model (Ravindran and Warsing, 2013; Nahmias, 2015; SAS, 2017; Hyndman and Athanasopoulos, 2018)

Seasonal ARIMA model is written with the general expression ARIMA $(p, d, q)(P, D, Q)_s$. The symbol p is the order of the non-seasonal autoregressive component, d is the order of the differencing, q is the order of the non-seasonal moving-average process, P is the order of the seasonal autoregressive part, D is the order of the seasonal differencing, Q is the order of the seasonal moving-average process, and s is the duration of the seasonal cycle.

Let Y_t be a dependent time series $\{Y_t: 1 \leq t \leq n\}$ at time t, then the mathematical formula for seasonal ARIMA model is expressed as in Equation (3.3).

$$(1 - B)^d (1 - B^s)^D Y_t = \mu + \frac{\theta(B)\theta_s(B^s)}{\varphi(B)\emptyset_s(B^s)} \epsilon_t \tag{3.3}$$

where μ is the constant mean; B^s is the seasonal backward shift operator; $\emptyset_s(B^s) = 1 - \emptyset_{s,1}(B^s) - \cdots - \emptyset_{s,P}(B^{sP})$ is the seasonal autoregressive component; $\theta_s(B^s) = 1 - \theta_{s,1}(B^s) - \cdots - \theta_{s,Q}(B^{sQ})$ is the seasonal moving-average component.

3.1.5 Seasonal Exponential Smoothing Model (Ravindran and Warsing, 2013; Nahmias, 2015; SAS, 2017; Hyndman and Athanasopoulos, 2018)

In the seasonal exponential smoothing method (ESM), the equation of forecast value at time $t + k$ (Y_{t+k}) is given by Equation (3.4).

$$Y_{t+k} = L_t + S_{t-p+k} \tag{3.4}$$

The smoothing equations are given using Equations (3.5) and (3.6).

$$L_t = \alpha\left(X_t - S_{t-p}\right) + (1-\alpha)L_{t-1} \tag{3.5}$$

$$S_t = \gamma(X_t - L_t) + (1-\gamma)S_{t-p} \tag{3.6}$$

Where X_t is given observation at time t, and α and γ are the level and seasonal smoothing parameters respectively, L_t is the estimated level component at time t, S_t is the estimated seasonal component at time t and p is the periods after which the seasonal cycle repeats itself.

3.1.6 Multiplicative Holt-Winters Model (Ravindran and Warsing, 2013; Nahmias, 2015; SAS, 2017; Hyndman and Athanasopoulos, 2018)

The Holt-Winters model, also known as the triple exponential smoothing, applies three types of exponential smoothing to the time series - value, trend, and seasonality. The model equation for the Holt-Winters method can be either additive or multiplicative model. In this section, we present the multiplicative Holt-Winters model, whereas Section 3.1.7 presents the additive model.

The mathematical formula relevant to a time series with a trend and constant seasonal component using the Holt-Winters additive technique has the forecast at time $t + k$ (Y_{t+k}) given by Equation (3.7).

$$Y_{t+k} = (L_t + kT_t)SI_{t+k-p} \tag{3.7}$$

The smoothing equations are given using Equations (3.8) – (3.10).

$$L_t = \alpha\left(\frac{X_t}{SI_{t-p}}\right) + (1-\alpha)(L_{t-1} + T_{t-1}) \tag{3.8}$$

$$T_t = \beta(L_t - L_{t-1}) + (1-\beta)T_{t-1} \tag{3.9}$$

$$SI_t = \gamma\left(\frac{X_t}{L_t}\right) + (1-\gamma)SI_{t-p} \tag{3.10}$$

Where X_t is given observation at time t, α, β and γ are the level, trend and seasonal corresponding constants respectively, L_t is the estimated level at time t, T_t is the estimated trend at time t, SI_t is the seasonality index at time t, and p is the periods after which the seasonal cycle repeats itself.

3.1.7 Additive Holt-Winters Model (Ravindran and Warsing, 2013; Nahmias, 2015; SAS, 2017; Hyndman and Athanasopoulos, 2018)

For the additive model, the forecasted supply estimate for time $t + k$ is given by Equation (3.11).

$$Y_{t+k} = L_t + kT_t + S_{t-p+k} \tag{3.11}$$

The estimates of level, trend and seasonal factors for additive model equations are given using Equations (3.12) – (3.14).

$$L_t = \alpha\left(Y_t - S_{t-p}\right) + (1 - \alpha)(L_{t-1} + T_{t-1}) \tag{3.12}$$

$$T_t = \beta(L_t - L_{t-1}) + (1 - \beta)T_{t-1} \tag{3.13}$$

$$S_t = \gamma(Y_t - L_t) + (1 - \gamma)S_{t-p} \tag{3.14}$$

3.2 Machine Learning Algorithms

Machine learning is a subfield of computer science that evolved from the study of pattern recognition and computational learning theory in artificial intelligence. Moreover, Machine learning is a technology exploring the algorithms to analyze a set of data, learn from the insights gathered and make predictions on data (Srinivas and Rajendran, 2017).

Machine learning includes four types: (1) supervised machine learning, (2) semi-supervised learning, (3) unsupervised learning, and (4) reinforcement learning. Supervised machine learning techniques automatically based on a set of historical examples, or instances to determine a model of the relationship between a set of descriptive features and a target feature. We can then use this model to make predictions for new instances. These two separate steps are shown in Figure 3.2 (Kelleher et al., 2015).

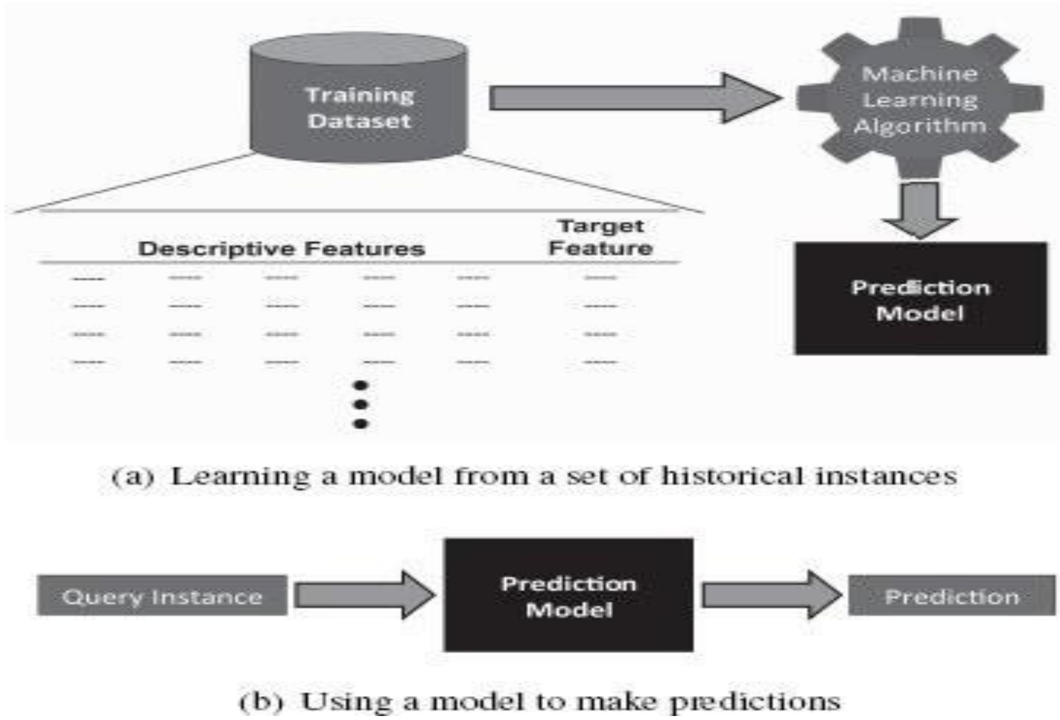


Figure 3.2: The Two steps in Supervised Machine Learning (Adapted from Kelleher et al., 2015)

For the blood supply forecasting, we leverage the two most widely used machine-learning techniques, artificial neural network and regression.

3.2.1 Artificial Neural Networks (ANN)

ANN is a reinforcement learning method that is an adaptation of a biological neural network. The network consists of several nodes that are distributed across numerous layers, and each layer is connected to its previous and subsequent layers within the network (Srinivas and Rajendran, 2017). These interconnected elements work closely to process information that they receive from the nodes of the previous layers and transfer them to the next layer based on the sigmoid function. They are particularly useful for modeling complex relationships in high-dimensional data or where the relationship between the input and output variables is not easy to understand (Srinivas and Rajendran, 2017).

3.2.2 Multiple Regression

Multiple regression is another class of problem in machine learning that is trying to predict a continuous value of a variable instead of a class, unlike in classification problem (Srinivas and Rajendran, 2017). Linear regression with ordinary least square is one of the classic machine learning algorithms in this domain. The mathematical formula for the regression model is represented in Equation (3.15).

$$Y = \beta_0 + \beta_1 X_1 + \cdots + \beta_n X_n + \epsilon \quad (3.15)$$

where Y is the response variable, X_n is a independent variable, β_0 is the intercept, β_i is the slope of the coefficient X_i (both β_0 and β_i are unknown coefficients to be estimated by the model), and ϵ is the error variable.

3.3 Evaluation of the Different Methods

Forecasting models play a critical role in many decision-making areas. After the model is selected, it is imperative to verify or validate the designed forecast model by comparing its forecasted data with historical data. We use four different measures of forecast errors for evaluating the model performance and the accuracy of the methods; they are MAE, MSE, BIAS and MAPE (Ravindran and Warsing, 2013; Chopra and Meindl, 2015; Nahmias, 2015).

Assume $X_1, X_{2,\ldots\ldots,} X_n$ are actual data, $F_1, F_{2,\ldots\ldots,} F_n$ are forecasted data, then the n values of forecast errors, $e_1, e_2, \ldots\ldots, e_n$, is given by: $e_1 = F_1 - X_1, e_2 = F_2 - X_{2,\ldots\ldots,} e_n = F_n - X_n$.

a) Mean Absolute Error (MAE) - measures the average significance of the forecast errors where all individual errors have equal weights.

$$MAE = \frac{1}{n}\sum_{i=1}^{n} |e_i|$$

b) Mean Squared Error (MSE) – also measures the significance of the forecast errors, larger errors get penalized more due to squaring.

$$MSE = \frac{1}{n}\sum_{i=1}^{n} e_i^2$$

c) BIAS: this is an indication of whether the forecast is overestimating or underestimating the actual supply over the forecast horizon.

$$BIAS = \sum_{i=1}^{n} e_i$$

d) Mean Absolute Percentage Error (MAPE) - measures the relative significance of forecasting errors in percentage terms.

$$MAPE = \frac{1}{n}\sum_{i=1}^{n} \left|\frac{e_i}{X_i}\right| \times 100$$

- *MAPE* is better than *MAE* since it takes into account the relative magnitude of the actual supply or demand and is also frequently used in practice.

3.4 Case Study

Some blood centers in Taiwan face blood shortage problems due to a lack of accurate forecasting of blood supply and demand (Taiwan Blood Services Foundation Statistics, 2017). In this case study, RBC (Red blood cell) supply data of one blood center have been collected and the data are analyzed for the time series forecasting.

3.4.1 Approach and Implementation

Once historical data have been gathered and analyzed in order to predict the future, the next step is to select a forecasting model for predicting. In the selection process, there are different and useful statistical and graphic techniques for the data analysis. First to graph sequence plots of the time series data for any time series forecasting analysis. A sequence plot is a graph of the data series values, usually on the vertical X axis, with time usually on the horizontal Y axis. The sequence plot will give the analyst an observable impression of the nature of the time series and suggest whether there are certain behavioral "components" present within the time series such as average level, trend, and seasonality.

First, calculate the 2013-2017 Weekly Supply Summary Statistics and the results are shown in Table 3.1 and Table 3.2.

Table 3.1: 2013-2017 TBSF Weekly Supply Summary Statistics

Year	Day	Average	Min.	Max.	Standard Deviation	Coefficient of Supply Variation (%)
2013	Sunday	188	32	461	84	44.68
	Monday	1,523	173	1,928	287	18.84
	Tuesday	820	154	1,558	200	24.39
	Wednesday	961	327	1,606	254	26.43
	Thursday	1,127	299	1,596	282	25.02
	Friday	1,039	458	1,956	263	25.31
	Saturday	135	43	462	68	50.37
2014	Sunday	174	31	456	82	47.13
	Monday	1,525	688	2,324	351	23.02
	Tuesday	858	327	1,935	253	29.49

Year	Day	Average	Min.	Max.	Standard Deviation	Coefficient of Supply Variation (%)
	Wednesday	857	168	1,474	210	24.50
	Thursday	1,238	80	2,048	304	24.56
	Friday	1,013	84	2,027	314	31.00
	Saturday	138	31	587	103	74.64
	Sunday	200	39	531	126	63.00
	Monday	1,504	850	2,636	303	20.15
	Tuesday	850	495	1,421	200	23.53
2015	Wednesday	855	1	1,461	252	29.47
	Thursday	1,381	139	1,923	309	22.38
	Friday	1,025	197	1,450	253	24.68
	Saturday	164	31	660	122	74.39
	Sunday	204	31	542	99	48.53
	Monday	1,497	162	2,073	331	22.11
	Tuesday	855	372	1,572	239	27.95
2016	Wednesday	862	146	1,264	199	23.09
	Thursday	1,439	547	2,643	319	22.17
	Friday	1,060	81	2,058	301	28.40
	Saturday	146	55	490	69	47.26
	Sunday	201	50	522	116	57.71
	Monday	1,445	212	1,964	324	22.42
	Tuesday	888	355	1,508	238	26.80
2017	Wednesday	888	272	1,656	224	25.23
	Thursday	1,383	502	1,846	273	19.74
	Friday	1,159	57	2,061	312	26.92
	Saturday	192	41	679	100	52.08

Table 3.2: 2013-2017 Weekday Average Supply Summary Statistics

	Average (Year)				
Year / Weekday	2013	2014	2015	2016	2017
Monday	1,523	1,525	1,504	1,497	1,445
Tuesday	820	858	850	855	888
Wednesday	961	857	855	862	888
Thursday	1,127	1,238	1,381	1,439	1,383
Friday	1,039	1,013	1,025	1,060	1,159
Saturday	135	138	164	146	192
Sunday	188	174	200	204	201

From Table 3.1 and Table 3.2, it is observed that the average blood supplies of the weekdays for each year are steady. Also, we can see that Monday supply is very high, Thursday and Friday supplies are quite high, Tuesday and Wednesday supplies are moderate, Saturday and Sunday supplies are significantly lower.

Implementation

- Used SAS software to analyze the data
- Leveraged built-in forecasting tools in SAS software
- Executed the model for one week (1/1/2018 – 1/7/2018)

3.5 Time-Series Forecasting Results

After running the seven different time series models discussed in Section 3.1 and obtaining the forecasts, we evaluate them using the error measures given in Section 3.3, and the results are presented in Table 3.3. It is clear that Seasonal ARIMA Model, Seasonal Exponential Smoothing Method and Multiplicative Holt-Winters Model yield minimal error measures. Hence, we conclude that, under the time series methods, these three models are the best forecasting the blood supply for the case study data under consideration.

Table 3.3: Error Measures Obtained under the Seven Time Series Models

Error	Method						
	AUTO REG	ARMA	Basic ARIMA	Seasonalized ARIMA	Seasonalized ESM	Multiplicative Holt-Winters	Additive Holt-Winters
MAE	215	449	600	160	158	159	159
MSE	88,031	288,002	577,197	57,235	57,111	57,111	57,189
BIAS	-383	-20,578	754	-5,575	-7,338	-8,507	-15,056
MAPE	94.50	227	224	80	81	81	80

Figure 3.3 to Figure 3.5 present Actual vs. Forecast, Prediction and 95% confidence level predictions (L95 and U95) of three best forecasting models.

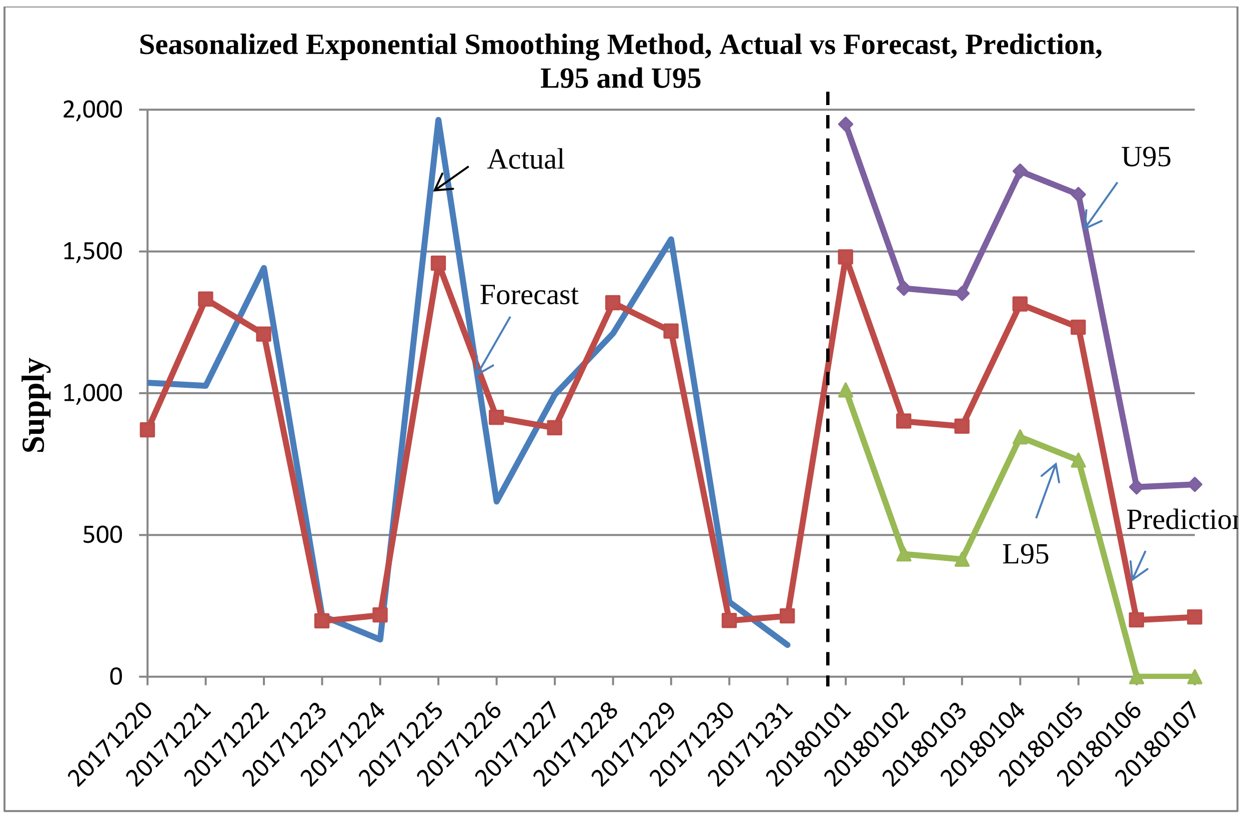


Figure 3.3: Seasonalized Exponential Smoothing Method

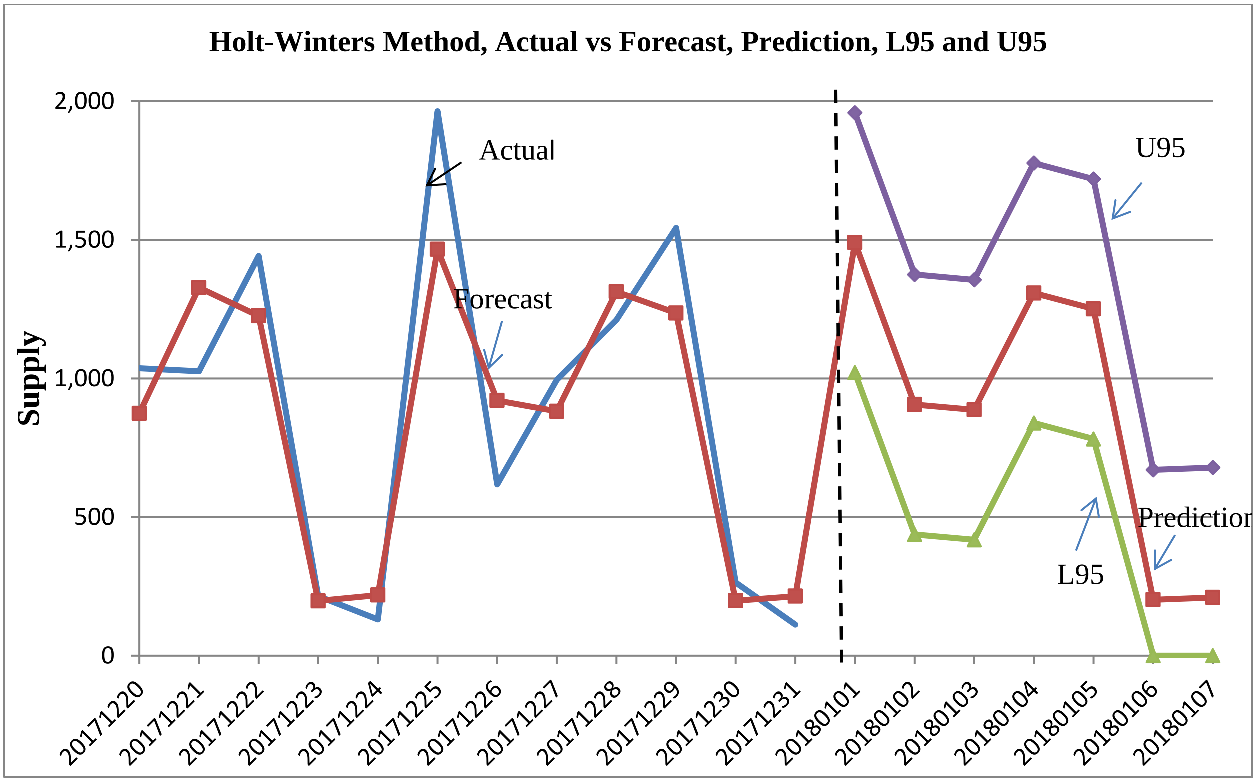


Figure 3.4: Multiplicative Holt-Winters Method

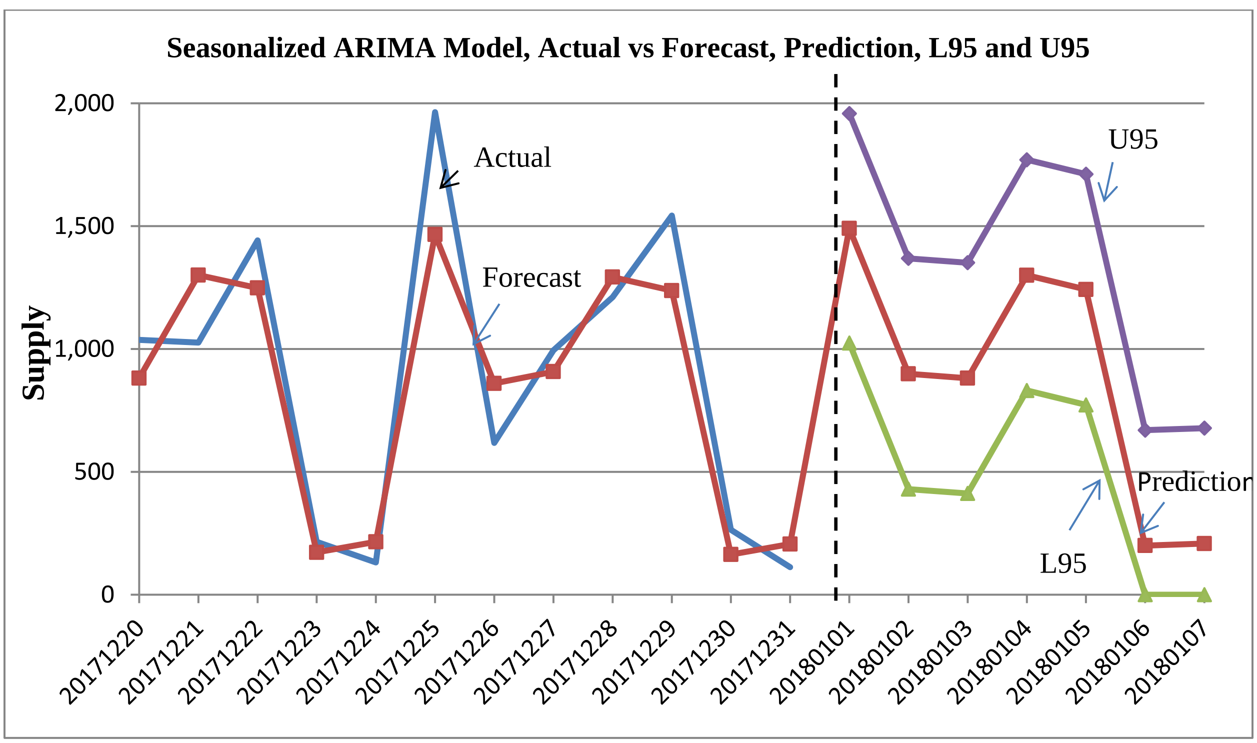


Figure 3.5: Seasonalized ARIMA Method Forecasting Model

3.6 Machine Learning Algorithm Results

The performance of the machine learning algorithms is compared in Table 3.4. For this particular dataset, results show that regression is a better predictor of the blood supply, nevertheless, the power of the results using regression is quite low (R^2 = 63.71%).

Table 3.4: Performance of Machine Learning Algorithms

Statistics of Fit	Artificial Neural Network	Regression
R-square	58.59%	63.71%

Therefore, regression is used to predict the supply for the first week of January 2018, as shown in Table 3.5. A summary of the results obtained under the time series method and regression is given in Table 3.5.

Table 3.5: Blood Supply Predictions using the Best Performing Time Series and Machine Learning Methods

Methods	**Prediction**						
	1/1/2018	1/2/2018	1/3/2018	1/4/2018	1/5/2018	1/6/2018	1/7/2018
Seasonalized ARIMA	1,491	899	882	1,301	1,242	200	208
Seasonalized ESM	1,480	901	883	1,314	1,232	200	210
Multiplicative Holt-Winters	1,490	906	887	1,308	1,251	202	210
Regression	1,458	1,269	1,088	951	779	589	410
Actual Supply	979	1,223	972	1,354	721	263	203

The machine learning neural networks are a complement to the familiar statistical tools of forecasting, but they are not a replacement for them (Montgomery et al., 2008). Clearly, from the results, we can infer that there is not a single method that predicts the supply accurately. Ravindran and Warsing (2013), Frances (2011) and (Gahirwal and Vijayalakshmi, 2013) suggest that the average supply of these three forecasting models produces a better forecasting, as shown in Table 3.6.

Table 3.6: Average Blood Prediction for 01/01/2018 to 01/07/2018 from Three Best Forecasting Models

Methods	Prediction						
	1/1/2018 Monday	**1/2/2018** Tuesday	**1/3/2018** Wednesday	**1/4/2018** Thursday	**1/5/2018** Friday	**1/6/2018** Saturday	**1/7/2018** Sunday
Seasonalized ESM	1,480	901	883	1,314	1,232	200	210
Multiplicative Holt-Winters Method	1,490	906	887	1,308	1,251	202	210
Seasonalized ARIMA Method	1,491	899	882	1,301	1,242	200	208
Average	**1,487**	**902**	**884**	**1,308**	**1,242**	**201**	**209**

3.7 Implications of Results

This case study focuses on predicting the supply of red blood cells for the Taiwan Blood Services Foundation (TBSF) (2019), a non-governmental and non-profit organization. So far, more than seven million citizens have donated blood in Taiwan through this foundation (which accounts for over 25% of the total population of Taiwan) (2019). Currently, blood centers at TBSF do not have a proper blood forecasting system, and some blood centers face blood shortage problems as a result of lack of accurate forecasting of blood supply. This paper focuses on developing a blood supply forecasting decision support tool for TBSF using time series and machine learning algorithms. The accurate forecasting models will enable TSBF to make good blood supply chain management planning decisions, such as when to collect blood from donors, how many units to collect, proper assignment of the workforce for collecting blood in donor drives, blood component testing process, etc. Upon accurately forecasting the future supply using the methods discussed in this study, inventory models can then be developed to make decisions on the number of units to order and time between orders.

There are some limitations to forecasting methods. The accuracy of forecasting could be affected by various factors. If there are some unknown variable(s) that could cause some of the fluctuations in the data, then it will be more difficult to forecast unless there are known explanatory variable(s) accounting for the variations. Blood supply forecasting is vital for blood supply chain decisions, and they are updated as more reliable information becomes available. Hence, after appropriate forecasting methods are selected, it is important to continuously monitor the forecast accuracy.

CHAPTER 4

BASIC BLOOD SUPPLY CHAIN MODEL UNDER DEMAND AND SUPPLY UNCERTAINTY INCORPORATING EMERGENCY DEMAND

4.1 Finite-Time Horizon Inventory (FTHI) Blood Supply Chain Model

An effective blood supply chain management (BSCM) should be capable of meeting the blood demand while reducing shortage costs and wastage costs. Demand and supply patterns can be generated from the historical demand and supply data or from a distribution based on the decision maker’s knowledge. Accompanying the blood supply and demand distribution patterns from historical data, we can plan blood collection schedules to coordinate and balance the blood demand and volunteer supply. In this section, a finite time horizon inventory (FTHI) model is presented to identify the optimal order quantity and time to order platelets such that wastage and shortages are reduced. A mixed-integer linear programming (MILP) model is developed, and the forecasted platelet supply and demand for the planning horizon derived from the historical data are given as inputs to the model. The overview of the Finite Time Horizon Model for Blood Supply Chain Inventory Management is shown in Figure 4.1.

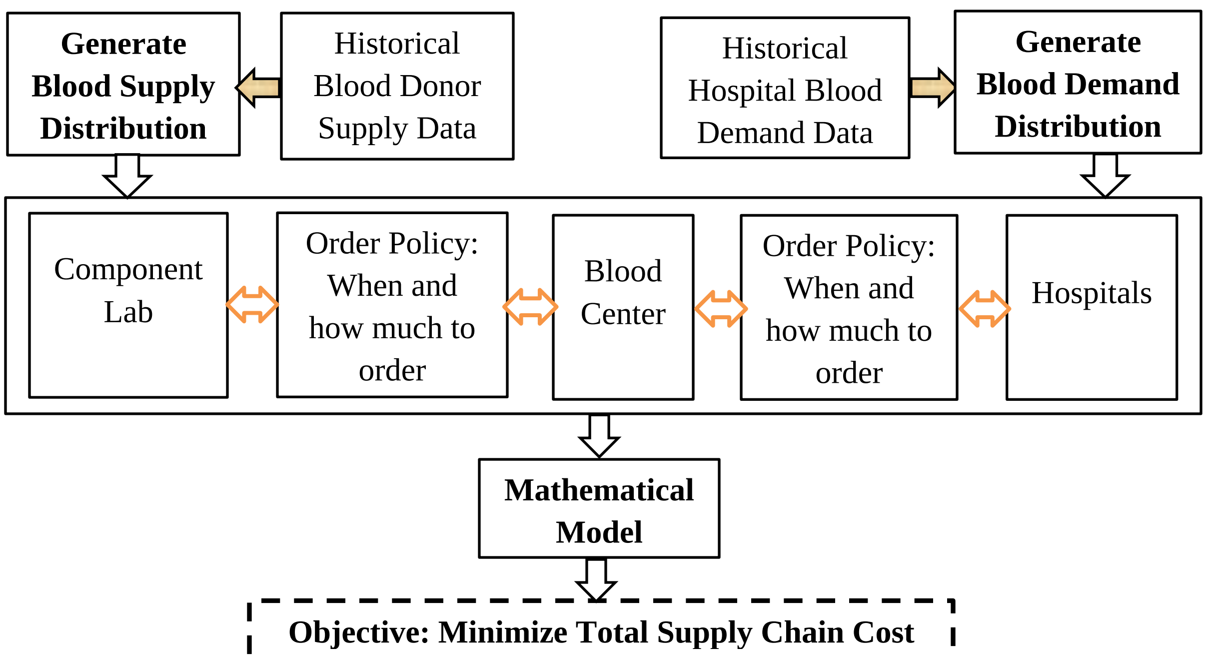


Figure 4.1: Overview of the Finite Time Horizon Blood Supply Chain Inventory Model

4.1.1 Blood Supply Chain Structure

Figure 4.2 presents a structure of the blood supply chain containing one blood center and a K number of hospitals. The regulations of the Health Insurance Portability and Accountability Act (HIPAA) ensure that each hospital can receive blood only from a designated blood center and cannot share or procure blood from other hospitals.

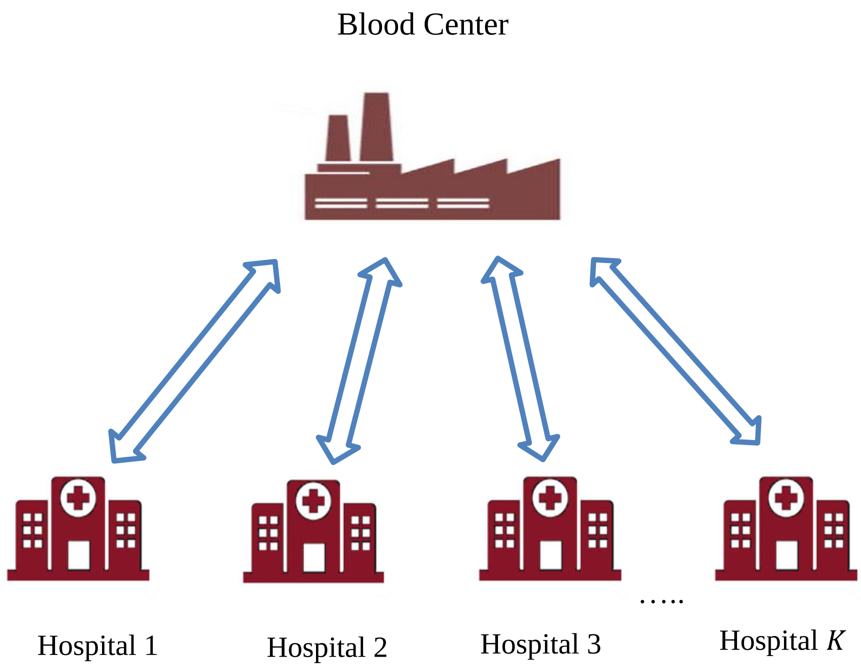


Figure 4.2: Structure of Supply Chain Containing One Blood Center and K Hospitals

Section 4.3 will describe how the blood demand flow between blood center and hospitals and a mathematical model for blood supply chain under blood and supply uncertainty is developed.

4.2 Model Assumptions

1. Lead time for the order processing is assumed to be negligible
2. All platelets arriving at hospital from the blood center are fresh and have a shelf life of three days
3. This model considers a single blood type
4. The FIFO issuing policy is applied at the hospital. That is, the platelet units with a one-day shelf life are first used for the demand fulfillment, then, two days and followed by three days shelf-life.

4.2.1 Scenario-Based Approach

The scenario optimization technique is utilized to solve the stochastic programming models by examining many possible circumstances for the platelet demand and supply. This approach is based on a set of key constraints for acquiring solutions to robust optimization problems. In a given period, each scenario corresponds to a specific combination of supply and demand patterns. It also relates to inductive reasoning in modeling and decision-making. Based on this stochastic programming approach, the number of acquired units with the regular shipments will remain the same, and the number of acquired units through emergency shipments (i.e., at times of shortage) and inventory is varied based on the scenario.

4.2.2 Notations for the Model

Parameters (known data) for the Model

l	Index of platelets shelf life (l =1,2,3)
k	Index of hospital k
s	Index of demand scenario (demand patterns for platelet) (s =1, 2, …, S)
t	Index of day t (t =1, 2, …, T)
K	Total number of hospitals (k =1, 2, …, K)
$pb(s)$	Probability of scenario s ($\sum_1^S pb(s) = 1$)
$foHP_k$	Fixed operating cost per day at the hospital k ($/day)
$fsHP_k$	Fixed shipping cost of purchasing platelets at hospital k ($/shipment)
$pcHP_k$	Platelet purchasing cost for each unit by hospital k ($)
$hcHP_k$	Holding cost for each inventory unit of platelet per day at hospital k ($/day/unit)
$ecHP_k$	Cost of outdated platelet for each unit at hospital k ($)
$scHP_k$	Shortage cost for each unit at hospital k ($) (This is referring to the procurement cost for each unit of platelet incurred through emergency shipment from the blood center)
$DEMAND_{k,t}(s)$	Platelet demand at hospital k at day t (units) under scenario s. The demand pattern can be estimated from historical data
$LTHP_k$	Lead time (days) of procurement at hospital k. It is the time between issuing orders for platelet and receiving the platelet. (Note: $LTHP_k$ = 0,1 or 2 only)
$RPHP_k$	Order review period at hospital k (days)
$iniHP_{k,l}$	Beginning inventory at the hospital k on day 1 with l days shelf life
$foBC$	Fixed operating cost per day incurred at the blood center ($/day)

$fsBC$	Fixed shipping cost per shipment of purchasing platelets associated with the blood center ($/shipment)
$pcBC$	Removal of platelet and testing cost for each unit associated with the blood center ($/unit)
$hcBC$	Inventory holding cost for each unit per day of platelet associated with the blood center ($/day)
$ecBC$	Cost of outdated platelet for each unit associated with the blood center ($/unit)
$scBC$	Shortage cost per unit ($/unit) associated with the blood center (this is referring to the procuring cost for each unit of platelet incurred through emergency shipment from other blood centers)
$SUPPLY_t(s)$	Platelet supply at blood center (units) at day t under scenario s. The supply pattern can be estimated from historical data.
$LTBC$	Lead time (days) for blood center procurement of platelets. It is the time between issuing orders and receiving fresh new platelets. It includes the time for collecting blood and two days for the testing time
$RPBC$	The review period for platelets ordering at the blood center (days)
$iniBC_l$	Beginning inventory at blood center on day one with l days shelf life

Main Decision Variables in association with the Model

$ORHP_{k,t}(s)$	At the end of day t, the number of platelet units ordered by hospital k, under scenario s
$REHP_{k,t,l}(s)$	At the start of day t, the number of units that hospital k obtained from the blood center with l days shelf life (l =1,2,3) from the blood center, under scenario s (note: the arriving platelets have the maximum shelf life of three days)
$OHHP_{k,t,l}(s)$	At the start of day t, the readily available inventory of platelet with l days shelf life (l =1, 2) at hospital k, under scenario s. Note: Since platelets possess a maximum shelf life of three days when they are delivered to the hospital, the inventory available at the start of day t (brought over from day t −1) can possess a maximum of two days shelf life.
$SHHP_{k,t}(s)$	At the end of day t, the shortage of platelet units at hospital k, under scenario s (note: these are procured units from the blood center through the request of emergency shipment by the hospital k)
$EXHP_{k,t}(s)$	At the end of day t, the expired platelet units at the hospital k, under scenario s

Main Decision Variables in association with the Blood Center for the Model

$ORBC_t(s)$	At the end of day t, platelet units procured by the blood drives under scenario s. The blood center will receive these ordered platelet units at the start of day t + $LTBC$
$REBC_t(s)$	At the start of day t, the total amount of platelet arriving from the component labs to the blood center upon the completion of the testing process, under scenario s (note that all units of platelet received by the blood center will be fresh new and possess a three days shelf life)
$BCTHP_{k,t,l}(s)$	On day t, units shipped to hospital k with the platelets with l days shelf life (l =1,2,3) from the blood center, under scenario s
$OHBC_{t,l}(s)$	At the start of day t, the on-hand units of platelet with l days shelf life (l =1, 2) at the blood center, under scenario s. Note: Since platelet units possess a maximum shelf life of three days, at the start of day t, the on-hand inventory (brought over from day t −1) can possess a maximum shelf life of two days.
$SHBC_t(s)$	At the end of day t, the shortage of platelets at the blood center under scenario s
$EXBC_t(s)$	At the end of day t, the number of expired platelet units at the blood center under scenario s

Objective Function in association with the Model

$TCSC$	Expected total cost gathered across the finite time (T) period for all scenarios of the blood supply chain

Figure 4.3 shows the blood demand and supply flow between one blood center and K hospitals.

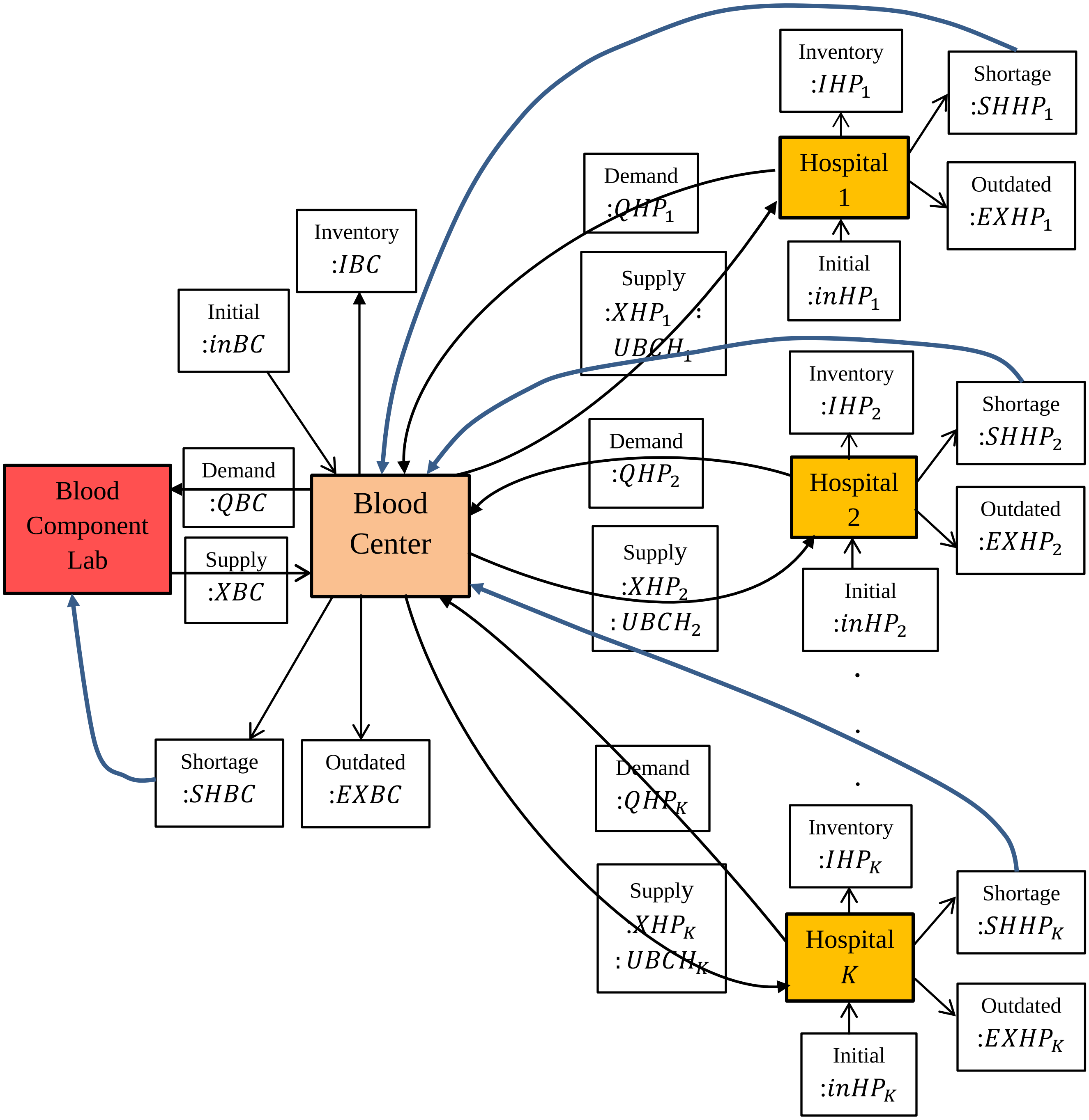


Figure 4.3: Blood Demand and Supply Flow between Blood Center and Hospitals

4.3 Stochastic Integer Linear Programming for the Blood Supply Chain

4.3.1 Sequence of Events at the Hospital

- Begin with the inventory of platelets with shelf lives of one-day and two-days
- Receive units of platelet from the blood center with one–, two– and three–day shelf lives
- Receive the demand for platelets
- Fulfill the platelet demand at the hospital in the following order:
  - ❖ Platelets with one-day shelf life are used first
  - ❖ If insufficient, the platelets with two-day shelf life are used next
  - ❖ Finally, the platelets with three-day shelf life are used
- At the end of the day, review the inventory of platelets and place orders for new platelets following the ordering policy.

4.3.2 Sequence of Events at the Blood Center

- Begin with the inventory of platelets with shelf lives of one-day and two-days
- Replenish stock with new platelets arriving from the component labs with a shelf life of three days.
- Receive regular demand from all the hospitals.
- Fulfill the hospital demands in the following platelets order:
  - ❖ Deliver platelets to hospital k with one-day shelf life first provided hospital k's lead time is zero days.
  - ❖ Next, deliver platelets to hospital k with two-day shelf life (if necessary) provided hospital k's lead time is zero or one day.
  - ❖ Finally, ship platelets to hospital k with a three-day shelf life (if necessary).
- Receive the demand for emergency from all hospitals
  - ❖ Deliver platelets to all hospitals placing emergency demand with a one-day shelf life first, followed by two-day and three-day shelf life platelets if necessary.
- Review the inventory of platelets at the end of the day and place orders for new platelets following the ordering policy.

4.4 Blood Supply Chain Model Formulation

Objective function: The objective of this model is to minimize the incurred total cost over the entire blood supply chain. There are 11 cost components associated with the entire blood supply chain:

- The cost associated with hospital k on day t:
  - ❖ Fixed operating cost: $foHP_k$
  - ❖ Fixed transportation cost: $fsHP_k \times binHP_{k,t}(s)$
  - ❖ Variable purchasing cost: $pcHP_k \times ORHP_{k,t}(s)$
  - ❖ Inventory holding cost: $hcHP_k \times \left(OHHP_{k,t,1}(s) + OHHP_{k,t,2}(s)\right)$
  - ❖ Shortage cost: $scHP_k \times SHHP_{k,t}(s)$
  - ❖ Expiration cost: $ecHP_k \times EXHP_{k,t}(s)$
- The cost related to the blood center on day t:
  - ❖ Fixed operating cost: $foBC$
  - ❖ Fixed transportation cost: $fsBC \times binBC_t(s)$
  - ❖ Inventory holding cost: $hcBC \times \left(OHBC_{t,1}(s) + OHBC_{t,2}(s)\right)$
  - ❖ Shortage cost: $scBC \times SHBC_t(s)$
  - ❖ Expiration cost: $ecBC \times EXBC_t(s)$

Note: Since this processing and testing cost will be covered by the various procurement costs paid by the hospitals, the objective function does not consider the cost of processing and testing platelets acquired at the blood center. To minimize the expected total cost across all scenarios over the entire blood supply chain under demand and supply uncertainty, the objective function is formulated as follows:

Minimize $TCSC =$

$$\sum_{t=1}^{T}\left[\sum_{s=1}^{S}\left[pb(s) \times \left\{\sum_{k=1}^{K}\left[foHP_k + fsHP_k \times binHP_{k,t}(s) + pcHP_k \times ORHP_{k,t}(s) + hcHP_k \times \left(OHHP_{k,t,1}(s) + OHHP_{k,t,2}(s)\right) + scHP_k \times SHHP_{k,t}(s) + ecHP_k \times EXHP_{k,t}(s)\right] + foBC \times t + fsBC \times binBC_t(s) + hcBC \times \left(OHBC_{t,1}(w) + OHBC_{t,2}(s)\right) + scBC \times SHBC_t(s) + ecBC \times EXBC_t(s)\right\}\right]\right] \quad (4.1)$$

$$REHP_{k,t,l}(s) = BCTHP_{k,t-LTHP_k,l+LTHP_k}(s) \qquad \forall\, t > LTHP_k \text{ and } l + LTHP_k \le 3 \qquad (4.2)$$

$$REHP_{k,t,l}(s) = 0 \qquad \text{Otherwise} \qquad (4.3)$$

$$DEMAND_{k,t}(s) - OHHP_{k,t,1}(s) - REHP_{k,t,1}(s) = RDHP_{k,t,1}(s) - LYHP_{k,t,1}(s) \quad \forall k,t,s \quad (4.4)$$

$$RDHP_{k,t,1}(s) - OHHP_{k,t,2}(s) - REHP_{k,t,2}(s) = RDHP_{k,t,2}(s) - LYHP_{k,t,2}(s) \quad \forall\, k,t,s \quad (4.5)$$

$$RDHP_{k,t,2}(s) - REHP_{k,t,3}(s) = RDHP_{k,t,3}(s) - LYHP_{k,t,3}(s) \quad \forall\, k,t,s \quad (4.6)$$

$$EXHP_{k,t}(s) = LYHP_{k,t,1}(s) \quad \forall\, k,t,s \quad (4.7)$$

$$OHHP_{k,t+1,1}(s) = LYHP_{k,t,2}(s) \quad \forall\, k,t,s \quad (4.8)$$

$$OHHP_{k,t+1,2}(s) = LYHP_{k,t,3}(s) \quad \forall\, k,t,s \quad (4.9)$$

$$SHHP_{k,t}(s) = RDHP_{k,t,3}(s) \quad \forall\, k,t,s \quad (4.10)$$

$$OHHP_{k,1,l}(s) = iniHP_{k,l} \quad \forall\, k,l,s \quad (4.11)$$

$$ORHP_{k,t,l}(s) = 0 \quad \forall\, k, t \ne RPHP_k, 2RPHP_k, \ldots, l, s \quad (4.12)$$

$$ORBC_t(s) = 0 \quad \forall\, t \ne RPBC, 2RPBC, \ldots, s \quad (4.13)$$

$$REBC_t(s) = ORBC_{t-LTBC}(s) \quad \forall\, t > LTBC, s \quad (4.14)$$

$$ORBC_t(s) = SUPPLY_t(s) \quad \forall\, t,s \quad (4.15)$$

$$\textstyle\sum_k BCTHP_{k,t,1}(s) + LFRBC_{t,1}(s) = OHBC_{t,1}(s) \quad \forall\, t,s, LTHP_k = 0 \quad (4.16)$$

$$\textstyle\sum_k BCTHP_{k,t,2}(s) + LFRBC_{t,2}(s) = OHBC_{t,2}(s) \quad \forall\, t,s, LTHP_k = 0{,}1 \quad (4.17)$$

(In general, $\sum_k BCTHP_{k,t,l}(s) + LFRBC_{t,l}(s) = OHBC_{t,l}(s) \;\; \forall\, t,s, and\ l = 1{,}2, LTHP_k \le l$)

$$\textstyle\sum_k HP3_{k,t}(s) + LFRBC_{t,3}(s) = REBC_t(s) \quad \forall\, t,s, LTHP_k = 0{,}1{,}2 \quad (4.18)$$

$$BCTHP_{k,t,1}(s) + BCTHP_{k,t,2}(s) + HP3_{k,t}(s) + SHRBC_{k,t}(s) = ORHP_{k,t}(s) \quad \forall\, t,k,s \quad (4.19)$$

$$BCTHP_{k,t,3}(s) = HP3_{k,t}(s) + SHRBC_{k,t}(s) \quad \forall\, t,k,s \quad (4.20)$$

$$\textstyle\sum_k SHHP_{k,t}(s) - LFRBC_{t,1}(s) = RSHBC_{t,1}(s) - LFEBC_{t,1}(s) \quad \forall\, t,s \quad (4.21)$$

$$RSHBC_{t,1}(s) - LFRBC_{t,2}(s) = RSHBC_{t,2}(s) - LFEBC_{t,2}(s) \quad \forall\, t,s \quad (4.22)$$

$$RSHBC_{t,2}(s) - LFRBC_{t,3}(s) = RSHBC_{t,3}(s) - LFEBC_{t,3}(s) \quad \forall\, t,s \quad (4.23)$$

$$SHEBC_t(s) = RSHBC_{t,3}(s) \quad \forall\, t,s \quad (4.24)$$

$$EXBC_t(s) = LFEBC_{t,1}(s) \quad \forall\, t,s \quad (4.25)$$

$$OHBC_{t+1,1}(s) = LFEBC_{t,2}(s) \quad \forall\, t,s \quad (4.26)$$

$$OHBC_{t+1,2}(s) = LFEBC_{t,3}(s) \quad \forall\, t,s \quad (4.27)$$

$$SHBC_t(s) = \textstyle\sum_k SHRBC_{k,t}(s) + SHEBC_t(s) \quad \forall\, t,s \quad (4.28)$$

$$OHBC_{1,l}(s) = \ iniBC_l \qquad \forall\ l, s \qquad (4.29)$$

$$REHP_{k,t,l}(1) = REHP_{k,t,l}(2) = \cdots = REHP_{k,t,l}(s) \qquad \forall k, t, l, s \qquad (4.30)$$

$$ORHP_{k,t,l}(1) = ORHP_{k,t,l}(2) = \cdots = ORHP_{k,t,l}(s) \qquad \forall k, t, l, s \qquad (4.31)$$

$$REHP_{k,t,1}(s) + REHP_{k,t,2}(s) + REHP_{k,t,3}(s) \leq M \times binHP_{k,t}(s) \qquad \forall k, t, s \qquad (4.32)$$

$$REBC_t(s) \leq M \times binBC_t(s) \qquad \forall\ t, s \qquad (4.33)$$

$$\begin{aligned}&REHP_{k,t,l}(s), RDHP_{k,t,l}(s), LYHP_{k,t,l}(s), OHHP_{k,t,l}(s), SHHP_{k,t}(s),\ \ ORHP_{k,t,l}(s),\\ &EXHP_{k,t}(s), LFRBC_{k,t,l}(s), BCTHP_{k,t,l}(s), HP3_{k,t}(s), REBC_t(s),\\ &SHRBC_{k,t}(s), LFEBC_{t,l}(s), OHBC_{t,l}(s), LBC_t(s), ORBC_t(s), SHEBC_t(s)\\ &SHBC_t(s), EXBC_t(s), RSHBC_t(s) \quad \geq\ 0 \qquad \forall l, k, t, s \qquad (4.34)\end{aligned}$$

$$binHP_{k,t}(s) = 0\ or\ 1 \qquad \forall k, t, s \qquad (4.35)$$

$$binBC_t(s) = 0\ or\ 1 \qquad \forall t, s \qquad (4.36)$$

(i) *Units of Platelet Obtained by the Hospital k from the Blood Center*

Constraint (4.2) states that the total units obtained from the blood center by the hospital k with a shelf-life of l days ($REHP_{k,t,l}(s)$), will be equivalent to the units delivered from the blood center on day $t - LTHP_k$, with a shelf life of $l + LTHP_k$ days is given by Equation (4.2). (Note: $LTHP_k$ = 0, 1 or 2 days)

(ii) *Uncertainty Demand-Inventory Balance at Hospital k and day t under Scenario s*

Constraint (4.4) states that at hospital k, if stochastic demand $DEMAND_{k,t}(s)$ is higher than the units of platelet with one-day shelf life (i.e.,$DEMAND_{k,t}(s) > OHHP_{k,t,1}(s) + REHP_{k,t,1}(s)$), then the remaining demand denoted by, $RDHP_{k,t,1}(s)$ is equal to $DEMAND_{k,t}(s)$ $-OHHP_{k,t,1}(s) - REHP_{k,t,1}(s)$ and leftover inventory with one-day shelf life denoted by, $LYHP_{k,t,1}(s)$ will be 0. On the other hand, if $DEMAND_{k,t}(s) \leq OHHP_{k,t,1}(s) + REHP_{k,t,1}(s)$ then $RDHP_{k,t,1}(s) = 0$ and $LYHP_{k,t,1}(s) = OHHP_{k,t,1}(s) + REHP_{k,t,1}(s) - DEMAND_{k,t}(s)$. Equation (4.4) is used to calculate $RDHP_{k,t,1}(s)$ and $LYHP_{k,t,1}(s)$.

- If $RDHP_{k,t,1}(s)$ is positive, then the platelet units with two days shelf life first fulfill the leftover demand (i.e., $OHHP_{k,t,2}(s) + REHP_{k,t,2}(s)$). If $RDHP_{k,t,1}(s) >\ OHHP_{k,t,2}(s) +$

$REHP_{k,t,2}(s)$, then leftover demand, $RDHP_{k,t,2}(s)$ will be equal to $RDHP_{k,t,1}(s) - OHHP_{k,t,2}(s) - REHP_{k,t,2}(s)$ and the remaining inventory with a shelf life of two days $LYHP_{k,t,2}(s)$ will be 0. On the other hand, if $RDHP_{k,t,1}(s) \leq OHHP_{k,t,2}(s) + REHP_{k,t,2}(s)$, then $RDHP_{k,t,2}(s)$=0 and the remaining platelets with two days shelf life is given by $LYHP_{k,t,2}(s) = OHHP_{k,t,2}(s) + REHP_{k,t,2}(s) - RDHP_{k,t,1}(s)$. Equation (4.5) is used to calculate $RDHP_{k,t,2}(s)$ and $LYHP_{k,t,2}(s)$.

- If $RDHP_{k,t,2}(s)$ is positive, then the fresh platelet units with three days shelf life (i.e., $REHP_{k,t,3}(s)$) first fulfills $RDHP_{k,t,2}(s)$. If $RDHP_{k,t,2}(s) > REHP_{k,t,3}(s)$, then the remaining demand, $RDHP_{k,t,3}(s)$ will be equal to $RDHP_{k,t,2}(s) - REHP_{k,t,3}(s)$ and the remaining inventory with three days shelf life, $LYHP_{k,t,3}(s)$ will be 0. If $RDHP_{k,t,2}(s) \leq REHP_{k,t,3}(s)$, then, $RDHP_{k,t,3}(s) = 0$, and the remaining platelets with three days shelf life is given by $LYHP_{k,t,3}(s) = REHP_{k,t,3}(s) - RDHP_{k,t,2}(s)$. Equation (4.6) is used to calculate $RDHP_{k,t,3}(s)$ and $LYHP_{k,t,3}(s)$.

The above-specified FIFO rules are established using Equations (4.4) – (4.6).

(iii) *Expired (Outdated) Platelet Units at the Hospital*

Constraint (4.7) states that at the end of day t, hospital k discards the unused platelet units with remaining shelf life of one day ($LYHP_{k,t,1}(s)$) and is given by Equation (4.7).

(iv) *Updates of Inventory at the Hospital*

The inventory at hospital j is updated at the end of each day using Equations (4.8) and (4.9). Note that the ending inventory is varied for each hospital based on the scenario.

(v) *Platelet Shortages at the Hospital*

Equation (4.10) represents the platelet shortages at the end of day t ($SHHP_{k,t}(s)$) which is the unfulfilled demand, $RDHP_{k,t,3}(s)$.

(vi) *Initial Inventory of Platelets at the Hospital*

Equation (4.11) represents the beginning inventory at each hospital k at time t = 1 under each scenario s.

(vii) *Platelet Units Ordered at the Hospital*

Equation (4.12) states that the hospital k can only order platelets at the time of the review periods ($t = RPHP_k, 2RPHP_k, \dots$), and cannot order platelets at the time of the other days.

(viii) *Units of Platelet Ordered and Received by the Blood Center*

Similar to Constraint (4.12), Equation (4.13) states that the blood center can only order platelets at the time of the review periods ($t = RPBC, 2RPBC, \dots$), and cannot order platelets at the time of the other days. At the blood center, upon the procedure of testing is complete, the total available units at the start of day t under scenario s ($REBC_t(s)$) are computed using Equations (4.14) and (4.15). It has to be equivalent to the ordered amount placed prior to the lead time ($ORBC_{t-LTBC}(s)$). Equations (4.15) states that the blood center has a stochastic supply at the start of each day t under scenario s, and the supply amount is estimated from historical real supply data.

(ix) *Fulfillment for the Regular Platelet Demand by the Blood Center*

Constraints (4.16) – (4.18) state that the total units of platelet distributed to the hospital k with l days shelf life on the day t ($BCTHP_{k,t,l}(s)$), are set as decision variables (i.e., the model determines the fulfillment policy for hospital demand), and they depend on the lead time of the hospital k. If the lead time at hospital k is one day, because of the expiration of platelets at the time of arrival at the medical center, then the platelet units with a one-day shelf life should not be delivered to hospital k from the blood center. Hence, if the lead time at hospital k is one day, then only platelet units must be distributed by the blood center should have two- or three-days shelf life. This is assured by Equations (4.16) and (4.17). Likewise, if the lead time is two days at hospital k, then only platelet units with three days shelf life have to be delivered to the hospital as given in Equation (4.18). However, if the lead time of hospital j is zero days, then the platelet units with a shelf life of any day can be shipped as given in Equations (4.16) – (4.18). As a result of the regular demand requested by hospital k, the platelets shortage encountered at the blood center ($SHRBC_{k,t}(s)$) is computed using Equation (4.19). As reviewed previously, this shortage units will be acquired from other blood centers and fulfilled to the blood center. Within the proposed model, it is presumed that the procured shortage units $SHRBC_{k,t}(s)$ will possess a three days shelf life. Therefore, although computing the platelet units which are delivered to the hospital by the blood center with the three-day shelf life category (i.e., $BCTHP_{k,t,3}(s)$), $SHRBC_{k,t}(s)$ should also be incorporated in alongside $HP3_{k,t}(s)$ (where $HP3_{k,t}(s)$ is the platelet units with three days shelf life from the available inventory delivered to the hospital k) as given in Equation (4.20).

<u>(x) *Fulfillment for the Emergency Demand by the Blood Center*</u>

Constraints (4.21) – (4.23) state that the *regular demand* placed by hospital k ($ORHP_{k,t}(s)$) must be satisfied with the blood center and the additional *emergency demand* requested on the same day t by that hospital ($SHHP_{k,t}(s)$) are also satisfied with the blood center. As indicated in Section 4.3 regarding the processing of daily events, upon the *regular demand* are fulfilled (i.e., $\sum_k SHHP_{k,t}\,(s)$ will be fulfilled with $\sum_l LFRBC_{t,l}\,(s)$), the *emergency demand* will be fulfilled only with inventory that is remaining Equations (4.21) – (4.23) are like equations for regular demand-inventory balance conditions previously discussed.

Note that $LFEBC_{t,l}(s)(l = 1,2,3)$ in constraints (4.21 - 4.23) represents the remaining inventory of platelet units, with one day, two days, and three days shelf life, upon completing the *emergency orders* of hospitals, and $RSHBC_{t,l}(s)(l = 1,2,3$ is the remaining shortage to be fulfilled by platelets. As a result of the emergency platelet demands requested by all the hospitals, the total shortage of platelets at the blood center is obtained by using Equation (4.24).

<u>(xi) *Expired (Outdated) Platelets at the Blood Center*</u>

At the end of each day t, the expired platelet units at the blood center are obtained by using Equation (4.25).

<u>(xii) *Updates of Inventory at the Blood Center*</u>

At the end of each day t, the inventory at the blood center is updated by using Equations (4.26) and (4.27).

<u>(xiii) *Platelet Shortages at the Blood Center*</u>

The platelet shortages at the blood center on each day t, under scenario s, gives the total scarcity as a result of the regular platelet demand ($\sum_k SHRBC_{k,t}\,(s)$) as well as the emergency demand ($SHEBC_t(s)$) requested by all the hospitals, as portrayed in Equation (4.28).

(xiv) *Initial Inventory of Platelets at the Blood Center*

Equation (4.29) gives the beginning inventory levels at the blood center at time $t = 1$ for each scenario s.

(xv) *Received units for hospital k have to be the same under all scenarios*

Equation (4.30) states that the received units for hospital k have to be the same for all scenarios over the supply chain planning horizon.

(xvi) *Ordered units for hospital k have equal amount under all scenarios over the planning horizon*

Equation (4.31) states that the ordered units for hospital k have an equal amount for all the scenarios over the planning horizon.

(xvii) *Total platelet units received by all hospitals shipped from the blood center*

Equation (4.32) gives the total platelet units with l days shelf life being received by all hospitals, at the start of day t.

(xviii) *Total platelet units delivered to the blood center from the component labs*

Equation (4.33) gives the total platelet units delivered from the component labs to the blood center upon the completion of the testing procedure, at the start of day t, under scenario s.

(xix) *Non-negative integer Constraints*

Constraints (4.34) represent non-negative integer constraints in the model. Constraints (4.35) – (4.36) correspond to non-negativity binary constraints within the model.

4.5 Computational Results

As discussed in Section 4.4, the model of the stochastic blood supply chain is programmed and solved using Python software with Gurobi Optimizer v8.1. The problem was solved to optimality for one blood center and two hospitals with a planning horizon of 300 days and 100 scenarios. It had 2,040,006 variables (90,000 are binary) and 1,621,202 constraints. It took about five minutes to process 417,279 iterations to solve the problem. Sections 4.5.1 and 4.6 discussed the results of computing solutions and sensitivity analysis in detail.

4.5.1 Base Case Results

This section examines the effectiveness of the developed stochastic mixed-integer programming model. Table 4.1 shows the base case parameter values, and these are based on the data given in the literature (Haijema, 2013; Civelek et al., 2015; Rajendran and Ravindran, 2017; Rajendran and Ravindran, 2019) for a setting with two hospitals and one blood center. The impact of these cost parameters on the performance measures is discussed in Section 4.6. Table 4.2 shows the performance measures and overall average cost measures for the base model with a planning horizon of 300 days and 100 scenarios. It is evident that Hospital #2 experiences more shortage, which is primarily because of the limited shelf life of arriving platelets. In other words, since the lead time for Hospital #2 is two days, there is comparatively more shortage and outdating observed in this hospital. As a result of the increased number of units purchased by Hospital #1, there are more units held in inventory, resulting in less shortage.

Table 4.1: Input Parameters for Base Case Setting

Input Parameter	Values		
Total Days Over Time Horizon	300		
Total Number of Scenarios	100		
Hospitals / Blood Center	Hospital 1	Hospital 2	Blood Center
Lead Time (days)	1	2	5
Review Period (days)	1	1	1
Fixed Cost of Procurement per Shipment	113	225	1,125
Inventory Holding Cost per Unit per Day	130	130	108
Variable Purchasing Cost per Unit ($)	650	650	538
Shortage Cost per Unit ($)	3,250	3,250	2,690
Outdating Cost per Unit ($)	650	650	538
Platelet Demand/Supply Distribution	$N \sim (200,32)$	$N \sim (100,16)$	$N \sim (225,36)$

Table 4.2: Average Performance Measures for Base Case Setting (T=300, S=100)

Performance Measure	Hospital 1	Hospital 2	Blood Center
Unit Shortage	14	23	41
Unit Outdating	0	1	0
Unit Holding	21	0	1
Unit Purchased	186	78	225
Fixed Cost	1.13	2.25	11.25
Demand/Supply	N ~ (200,32)	N ~ (100,16)	N ~ (225, 37)
Overall Measures			
Average Cost/per day/per scenario	Best	Worst	STD
4,068	3,800	4,264	84

4.6 Sensitivity Analysis

In this section, the impact of supply and demand parameters, as well as the cost settings, are varied to investigate their effects on performance measures, such as shortage, outdating, holding, units purchased, and total cost.

4.6.1 Impact of Changes in Demand and Supply Parameters

Table 4.3 shows the changes in coefficients of variation (CV) of both the supply can demand. The CV is varied from 10% to 50%, in steps of 0.1 at a time. Table 4.4 and Figures 4.4–4.6 show the impacts on average performance measures for hospital #1, #2, and the blood center, respectively. Clearly, we can see that units outdated, held in inventory, and shortage increase with the inflation in the CV. Unexpectedly, the total units purchased decreases with the rise in CV for both the hospitals, which may be primarily because of the variations of demand for both the hospitals. The average supply at the blood center remains almost the same across the different CV settings, and is approximately equal to the mean. Table 4.5 and Figure 4.7 show the overall average cost measures for different coefficients of demand and supply variations. Clearly, we can see that the average total supply chain cost increases with the increase in the CV.

Table 4.3: Coefficients of Variation (CV) of Supply and Demand Settings

Setting	Hospital 1	Hospital 2	Blood Center
CV1 (CV=0.1)	$N\sim(200,20)$	$N\sim(100,10)$	$N\sim(225,23)$
CV2 (CV=0.2)	$N\sim(200,40)$	$N\sim(100,20)$	$N\sim(225,45)$
CV3 (CV=0.3)	$N\sim(200,60)$	$N\sim(100,30)$	$N\sim(225,68)$
CV4 (CV=0.4)	$N\sim(200,80)$	$N\sim(100,40)$	$N\sim(225,90)$
CV5 (CV=0.5)	$N\sim(200,100)$	$N\sim(100,50)$	$N\sim(225,113)$

Table 4.4 illustrates the impacts for different coefficients of demand variation

Table 4.4: Impacts of different Coefficients of Demand Variation

	Base			**CV=0.1**		
Performance Measure	**Hospital 1**	**Hospital 2**	**Blood Center**	**Hospital 1**	**Hospital 2**	**Blood Center**
Unit Shortage	14	23	41	17	21	36
Unit Outdating	0	1	0	0	0	0
Unit Holding	21	0	1	4	0	0
Unit Purchased	186	78	225	183	79	225
Fixed Cost	1.13	2.25	11.25	1.13	2.25	11.25

	CV=0.2			**CV=0.3**		
Performance Measure	**Hospital 1**	**Hospital 2**	**Blood Center**	**Hospital 1**	**Hospital 2**	**Blood Center**
Unit Shortage	15	25	42	18	29	46
Unit Outdating	0	1	0	2	3	0
Unit Holding	30	0	2	43	0	6
Unit Purchased	185	76	225	184	74	225
Fixed Cost	1.13	2.25	11.25	1.13	2.25	11.25

	CV=0.4			CV=0.5		
Performance Measure	**Hospital 1**	**Hospital 2**	**Blood Center**	**Hospital 1**	**Hospital 2**	**Blood Center**
Unit Shortage	24	34	51	30	39	56
Unit Outdating	5	5	0	8	8	0
Unit Holding	45	0	12	45	0	18
Unit Purchased	181	72	225	178	69	226
Fixed Cost	1.13	2.25	11.25	1.13	2.25	11.25

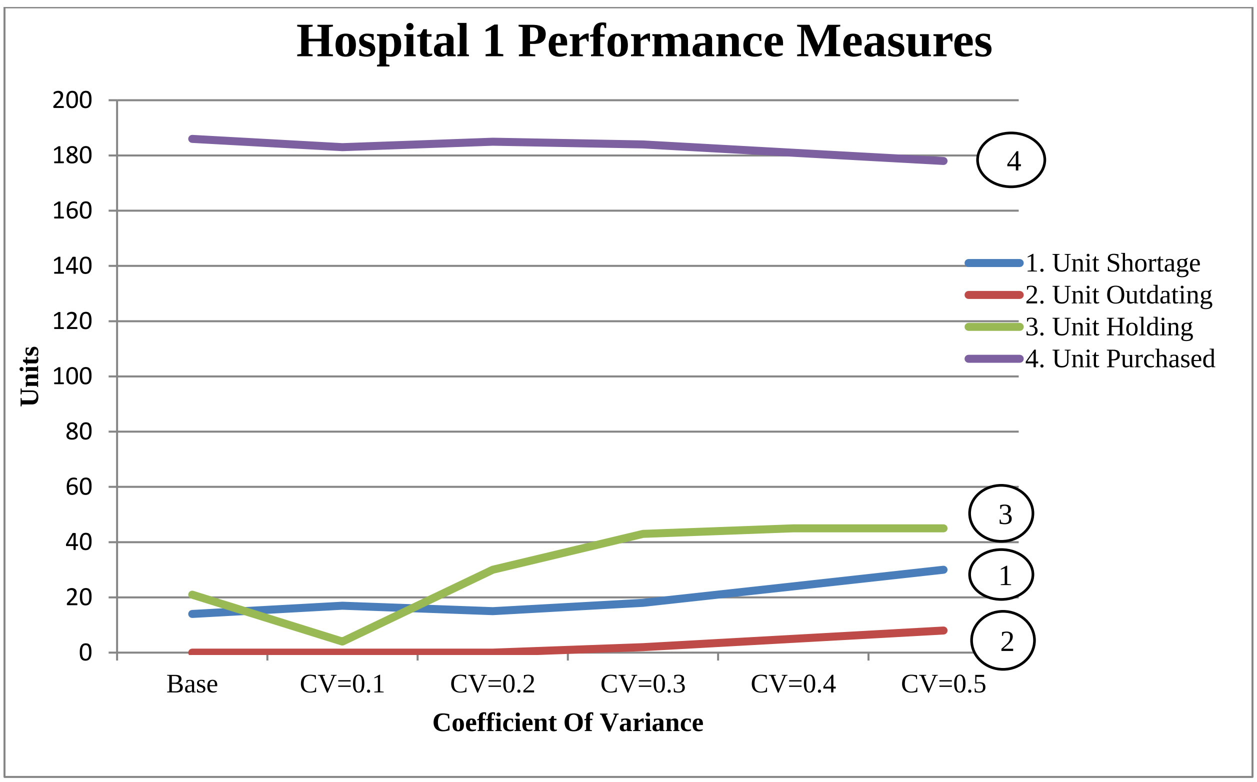


Figure 4.4: Impact of CV on Performance Measures of Hospital 1

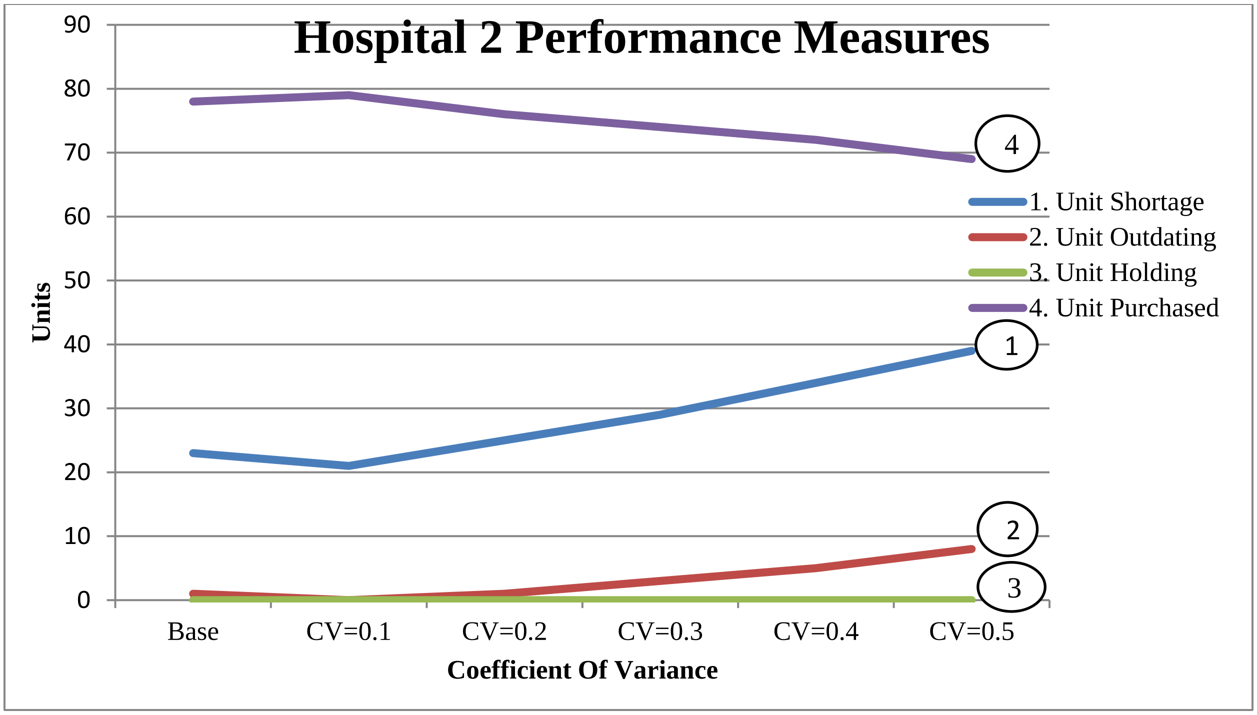


Figure 4.5: Impact of CV on Performance Measures of Hospital 2

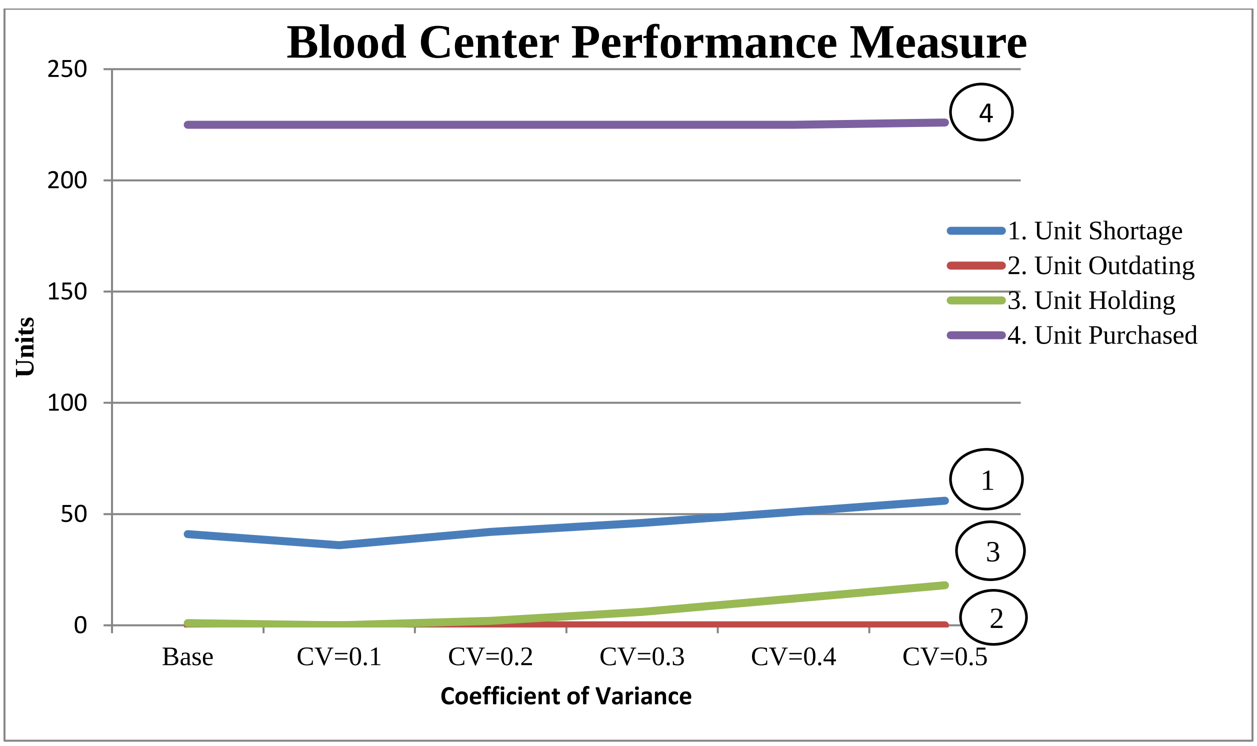


Figure 4.6: Impact of CV on Performance Measures of Blood Center

Table 4.5: Impact of CV on the Total Supply Chain Cost

Overall Measures				
Settings	Average Cost/per day/per scenario	Best	Worst	STD
Base	4,068	3,800	4,264	84
CV=0.1	3,953	3,830	4,059	48
CV=0.2	4,177	3,879	4,436	93
CV=0.3	4,557	4,306	4,857	116
CV=0.4	5,040	4,713	5,455	155
CV=0.5	5,543	5,039	5,975	185

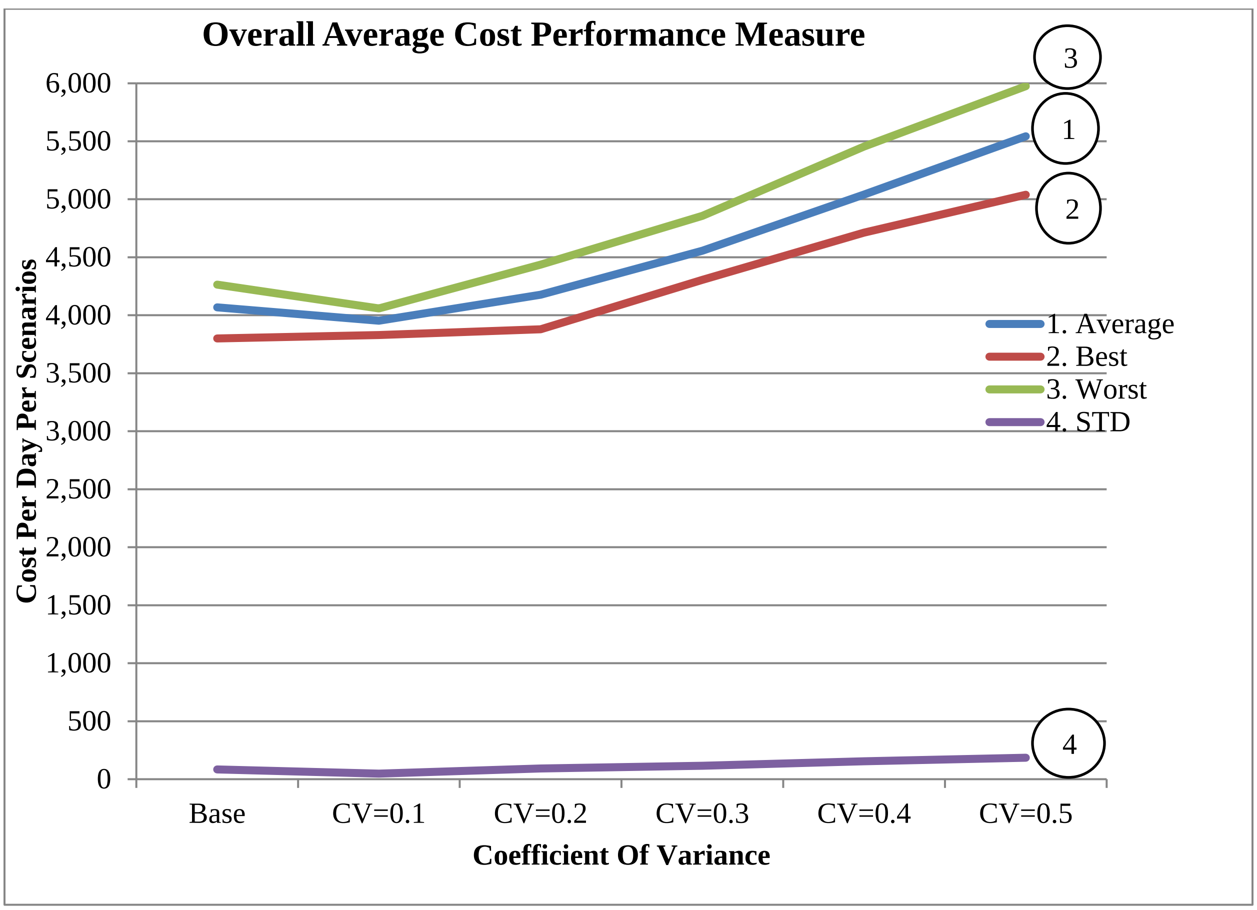


Figure 4.7: Overall Average Cost Performance Measure

4.6.2 Impact of Changes in the Cost Settings

Table 4.6 shows the different cost settings used for this analysis (adapted from Rajendran and Ravindran, 2019). Setting CSET1 represents the base case. Settings CSET2 – CSET9 are obtained by multiplying the different cost parameters by 0.5, whereas settings CSET10 – CSET17 are obtained by multiplying the different cost parameters by 1.5. Tables 4.7 – 4.10 show the impacts on average cost measures by different cost settings for different members of the supply chain. Table 4.11 shows the overall average cost performance measure by different cost settings. It is evident that

- Settings with shortage cost variations have the maximum deviation from the base case.
- The next most significant impact is observed for purchasing cost parameter alteration. This is expected because the purchasing cost has the maximum impact on the total cost.
- Due to the limited units outdated, the impact of varying the outdating cost parameters results in an insignificant change in total cost. A similar pattern is observed for holding cost variations, as well.

Table 4.6: Different Settings of the Cost

Cost Settings	Blood center			Hospital						
	Inventory holding cost /unit/day	Shortage cost/unit	Outdated cost/unit	Fixed cost/ shipment		Inventory holding cost /unit/day	Purchasing cost/unit	Shortage cost/unit	Outdated cost/ unit
				H1	H2				
CSET1 (base)	108	2,690	538	(113,225)		130	650	3,250	650
CSET2	**54**	2,690	538	(113,225)		130	650	3,250	650
CSET3	108	**1,345**	538	(113,225)		130	650	3,250	650
CSET4	108	2,690	**269**	(113,225)		130	650	3,250	650
CSET5	108	2,690	538	(**57,113**)		130	650	3,250	650
CSET6	108	2,690	538	(113,225)		**65**	650	3,250	650
CSET7	108	2,690	538	(113,225)		130	**325**	3,250	650
CSET8	108	2,690	538	(113,225)		130	650	**1,625**	650
CSET9	108	2,690	538	(113,225)		130	650	3,250	**325**
CSET10	**162**	2,690	538	(113,225)		130	650	3,250	650

CSET11	108	**4,035**	538	(113,225)	130	650	3,250	650
CSET12	108	2,690	**807**	(113,225)	130	650	3,250	650
CSET13	108	2,690	538	(**170,338**)	130	650	3,250	650
CSET14	108	2,690	538	(113,225)	**195**	650	3,250	650
CSET15	108	2,690	538	(113,225)	130	**975**	3,250	650
CSET16	108	2,690	538	(113,225)	130	650	**4,875**	650
CSET17	108	2,690	538	(113,225)	130	650	3,250	**975**

Table 4.7 Illustrates the impacts of different cost settings

Table 4.7: Impacts of different Cost Settings

	CS1 (Base)			**CS2**		
Performance Measure	**Hospital 1**	**Hospital 2**	**Blood Center**	**Hospital 1**	**Hospital 2**	**Blood Center**
Unit Shortage	14	23	41	14	23	41
Unit Outdating	0	1	0	0	1	0
Unit Holding	20	0	1	20	0	1
Unit Purchased	186	78	225	186	77	225
Fixed Cost	1.13	2.25	11.25	1.13	2.25	11.25

	CS3			**CS4**		
Performance Measure	**Hospital 1**	**Hospital 2**	**Blood Center**	**Hospital 1**	**Hospital 2**	**Blood Center**
Unit Shortage	5	10	65	14	23	41
Unit Outdating	1	4	0	0	1	0
Unit Holding	46	0	0	20	0	1
Unit Purchased	196	93	225	186	78	225
Fixed Cost	1.13	2.25	11.25	1.13	2.25	11.25

	CS5			CS6		
Performance Measure	**Hospital 1**	**Hospital 2**	**Blood Center**	**Hospital 1**	**Hospital 2**	**Blood Center**
Unit Shortage	14	23	41	11	24	43
Unit Outdating	0	1	0	0	0	0
Unit Holding	21	0	1	27	0	0
Unit Purchased	186	77	225	188	77	225
Fixed Cost	1.13	2.25	11.25	1.13	2.25	11.25

	CS7			CS8		
Performance Measure	**Hospital 1**	**Hospital 2**	**Blood Center**	**Hospital 1**	**Hospital 2**	**Blood Center**
Unit Shortage	11	19	48	48	40	9
Unit Outdating	0	1	0	0	0	0
Unit Holding	28	0	1	1	0	1
Unit Purchased	189	82	225	152	61	225
Fixed Cost	1.13	2.25	11.25	1.13	2.25	11.25

	CS9			CS10		
Performance Measure	**Hospital 1**	**Hospital 2**	**Blood Center**	**Hospital 1**	**Hospital 2**	**Blood Center**
Unit Shortage	14	23	42	14	23	41
Unit Outdating	0	1	0	0	1	0
Unit Holding	20	0	1	21	0	0
Unit Purchased	186	78	225	186	78	225
Fixed Cost	1.13	2.25	11.25	1.13	2.25	11.25

	CS11			CS12		
Performance Measure	**Hospital 1**	**Hospital 2**	**Blood Center**	**Hospital 1**	**Hospital 2**	**Blood Center**
Unit Shortage	28	35	21	14	23	41
Unit Outdating	0	0	0	0	1	0
Unit Holding	6	0	1	20	0	1
Unit Purchased	172	66	225	186	78	225
Fixed Cost	1.13	2.25	11.25	1.13	2.25	11.25

	CS13			CS14		
Performance Measure	**Hospital 1**	**Hospital 2**	**Blood Center**	**Hospital 1**	**Hospital 2**	**Blood Center**
Unit Shortage	14	23	41	16	23	40
Unit Outdating	0	1	0	0	1	0
Unit Holding	20	0	1	16	0	1
Unit Purchased	186	78	225	184	78	224
Fixed Cost	1.13	2.25	11.25	1.13	2.25	11.25

	CS15			CS16		
Performance Measure	**Hospital 1**	**Hospital 2**	**Blood Center**	**Hospital 1**	**Hospital 2**	**Blood Center**
Unit Shortage	19	28	33	5	11	63
Unit Outdating	0	0	0	1	3	0
Unit Holding	13	0	1	51	0	0
Unit Purchased	181	72	225	196	91	225
Fixed Cost	1.13	2.25	11.25	1.13	2.25	11.25

	CS17		
Performance Measure	**Hospital 1**	**Hospital 2**	**Blood Center**
Unit Shortage	14	23	40
Unit Outdating	0	0	0
Unit Holding	20	0	1
Unit Purchased	186	77	226
Fixed Cost	1.13	2.25	11.25

Table 4.8: Impacts of Cost Settings on Hospital 1

Average Performance Measures					
	Unit Shortage	Unit Outdating	Unit Holding	Unit Purchased	Total cost
CSET1(Base)	14	0	20	186	1,689
CSET2	14	0	20	186	1,691
CSET3	5	1	46	196	1,494
CSET4	14	0	20	186	1,692
CSET5	14	0	21	186	1,686
CSET6	11	0	27	188	1,617
CSET7	11	0	28	189	1,002
CSET8	48	0	1	152	1,773
CSET9	14	0	20	186	1,685
CSET10	14	0	20	186	1,689
CSET11	28	0	6	172	2,048
CSET12	14	0	20	186	1,689
CSET13	14	0	20	186	1,691
CSET14	16	0	16	184	1,758
CSET15	19	0	13	181	2,388
CSET16	5	1	51	196	1,570
CSET17	14	0	20	186	1,688

Table 4.9: Impacts of Cost Settings on Hospital 2

Average Performance Measures					
	Unit Shortage	Unit Outdating	Unit Holding	Unit Purchased	Total cost
CSET1(Base)	23	1	0	78	1,254
CSET2	23	1	0	77	1,261
CSET3	10	4	0	93	963
CSET4	23	1	0	78	1,262
CSET5	23	1	0	77	1,261
CSET6	24	0	0	77	1,280
CSET7	19	1	0	82	895
CSET8	40	0	0	61	1,037
CSET9	23	1	0	78	1,257
CSET10	23	1	0	78	1,260
CSET11	35	0	0	66	1,553
CSET12	23	1	0	78	1,255
CSET13	23	1	0	78	1,256
CSET14	23	1	0	78	1,247
CSET15	28	0	0	72	1,612
CSET16	11	3	0	91	1,173
CSET17	23	1	0	77	1,269

Table 4.10: Impacts of Cost Settings on Blood Center

Average Performance Measures					
Setting	Unit Shortage	Unit Outdating	Unit Holding	Unit Purchased	Total cost
CSET1(Base)	41	0	1	225	1,125
CSET2	41	0	1	225	1,125
CSET3	65	0	0	225	888
CSET4	41	0	1	225	1,125
CSET5	41	0	1	225	1,103
CSET6	43	0	0	225	1,156
CSET7	48	0	1	225	1,302
CSET8	9	0	1	225	255
CSET9	42	0	1	225	1,132
CSET10	41	0	0	225	1,128
CSET11	21	0	1	225	878
CSET12	41	0	1	225	1,123
CSET13	41	0	1	225	1,117
CSET14	40	0	1	224	1,100
CSET15	33	0	1	225	905
CSET16	63	0	0	225	1,714
CSET17	40	0	1	226	1,094

Table 4.11: Overall Average Cost Performance Measures by different Cost Settings.

Overall Average Cost Measures				
	Average	**Best**	**Worst**	**STD**
CSET1(Base)	4,068	3,800	4,264	84
CSET2	4,077	3,869	4,240	71
CSET3	3,345	3,232	3,465	51
CSET4	4,061	3,874	4,292	88
CSET5	4,073	3,897	4,259	76
CSET6	4,053	3,862	4,270	84
CSET7	3,199	3,044	3,377	74
CSET8	3,065	2,964	3,180	46
CSET9	4,074	3,906	4,226	81
CSET10	4,077	3,889	4,242	68
CSET11	4,479	4,268	4,668	86
CSET12	4,066	3,879	4,273	70
CSET13	4,064	3,821	4,357	88
CSET14	4,105	3,882	4,374	90
CSET15	4,904	4,647	5,109	75
CSET16	4,457	4,234	4,758	95
CSET17	4,051	3,856	4,249	82

4.7 Case Study

A stochastic process is simply a collection of random variables labeled by some parameter. A scenarios is any possible set of values for the stochastic variables. Any stochastic (random) process can be represented by a number of scenarios. As we would expect, the higher the number of scenarios considered, the more appropriate is the representation of the stochastic process, at the expense of more challenging mathematical model to be solved. (Tarim et al., 2006, Ravindran, 2008, Niknam et al., 2012, Dillon et al., 2017)

Define a set of *S* future scenarios and assign likelihood *p(s)* that scenario *s* will occur. For example,

Scenarios (s)	Likelihood $(p(s))$	$Expected_t$
$SUPPLY_t(1)$	$ps(1)$	
$SUPPLY_t(2)$	$ps(2)$	
$\dots$	$\dots$	

$SUPPLY_t(S_s)$	$ps(S_s)$	$\sum_{s=1}^{S_s} SUPPLY_t(s) * ps(\mathrm{s})$
$DEMAND_{h,t}(1)$	$pd(1)$	
$DEMAND_{h,t}(2)$	$pd(2)$	
…	…	
$DEMAND_{h,t}(S_d)$ (h is for hospital)	$pd(S_d)$	$\sum_{s=1}^{S_d} DEMAND_{h,t}(s) * pd(\mathrm{s})$ (h is for hospital)

The scenario approach or scenario optimization approach is a technique for obtaining solutions to robust optimization and chance-constrained optimization problems. The scenario-based optimization technique is utilized in the proposed model to solve the stochastic programming models by examining many possible circumstances for the platelet demand and supply. This approach is based on a set of key constraints for acquiring solutions to robust optimization problems. In a given period, each scenario corresponds to a specific combination of supply and demand patterns. Based on this stochastic programming approach, the number of acquired units with the regular shipments will remain the same, and the number of acquired units through emergency shipments (i.e., at times of shortage) and inventory is varied based on the scenario.

Assume the supply and demand have the same weekly normal distributions. (Rajendran and Srinivas, 2020). From Table 3.2 in chapter 3: 2013-2017 Weekday Average Supply Summary Statistics is shown as below:

	Average (Year)					
Year / **Weekday**	**2013**	**2014**	**2015**	**2016**	**2017**	**Mean**
Sunday	188	174	200	204	201	193
Monday	1,523	1,525	1,504	1,497	1,445	1,499
Tuesday	820	858	850	855	888	854
Wednesday	961	857	855	862	888	885
Thursday	1,127	1,238	1,381	1,439	1,383	1,314
Friday	1,039	1,013	1,025	1,060	1,159	1,059
Saturday	135	138	164	146	192	155

For the case study, it is assumed that the weekday has same Demand and Supply Distribution which is shown as in Figure 4.8 and Table 4.12

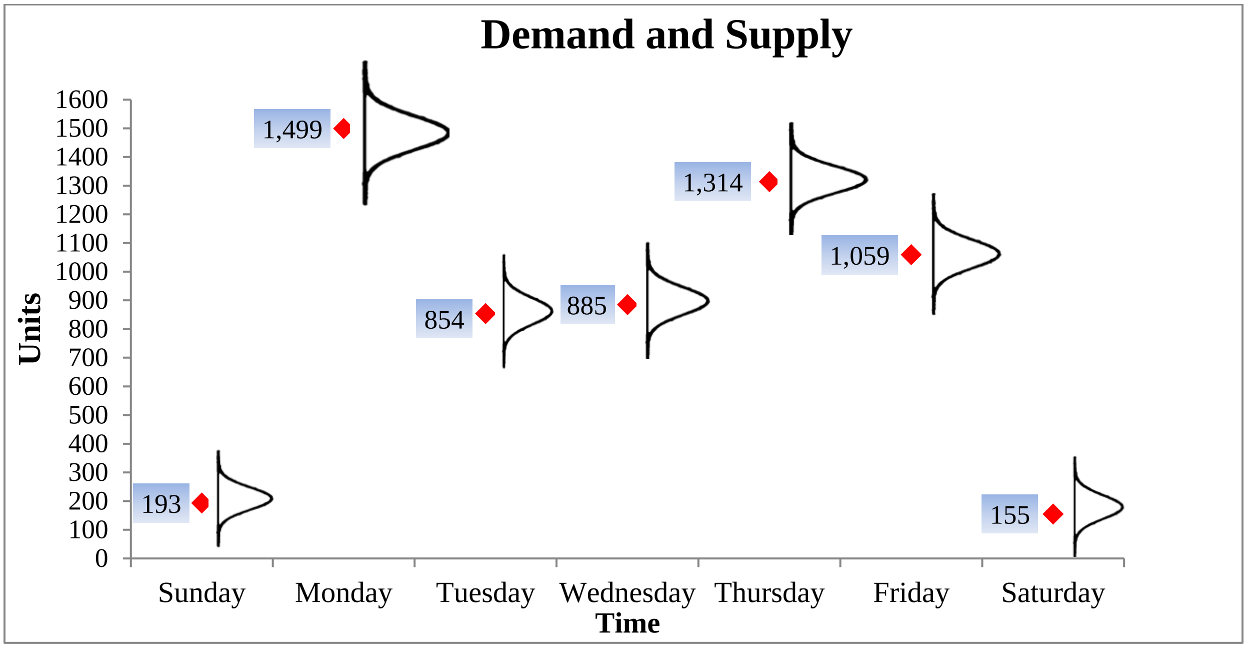


Figure 4.8: Weekday Demand and Supply Distribution

Table 4.12: Weekday Demand and Supply Distribution

	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
Mean	193	1,499	854	885	1,314	1,059	155
Demand /Supply	N ~ (193,19)	N ~ (1499,150)	N ~ (854,85)	N ~ (885, 89)	N ~ (1314,131)	N ~ (1059,106)	N ~ (155,16)

Solving the stochastic programming models, the weekday blood ordering units, holding units, outdating units, and shortage units, etc. for two hospitals and one blood center are shown in Tables 4.13, 4.14, and 4.15. The overall performance measure by weekday is shown in Table 4.16.

4.7.1 Weekday Implementation Results of Case Study

Tables 4.13 to 4.15 and Figures 4.9 to 4.11 show the impacts of demand and supply distribution on average weekday performance measures for hospital #1, #2, and the blood center, respectively. Clearly, we can see that units purchased, outdated, held in inventory, and shortage varied with the inflation in the demand and supply. Table 4.16 and Figure 4.12 show the overall average cost measures for weekday of demand and supply variations. It is shown that the average total supply chain cost varied with the inflation in the demand and supply. From the results, it is evident that

- Since there are initial inventories at beginning of the week, there are not many units to order for hospital 1 and hospital 2, the blood center has purchased some units, there is no purchased costs occurred for blood center, the average total supply chain cost is moderate.
- The purchased units are low for Saturday and Sunday comparing with Tuesday, Wednesday, Thursday, and Friday, this is expected because low demand for Saturday (N ~ (155,16)) and Sunday N ~ (193,19), the average total supply chain cost for Saturday and Sunday have the minimum weekday cost.
- Clearly, as the overall performance measures by weekday for Tuesday, Wednesday, Thursday and Friday shown in Table 4.16 and Figure 4.12, we can see that the average total supply chain cost increase with the inflation in the demand and supply. Due to the nature of stochastic process, the best and worst overall performance measures by weekday result in a significant difference in total cost. A similar pattern is observed for cost standard deviation by weekday, as well.

Table 4.13: Average Performance Measures for Hospital 1

	Hospital 1						
Performance Measure	**Monday**	**Tuesday**	**Wednesday**	**Thursday**	**Friday**	**Saturday**	**Sunday**
Unit Shortage	3	36	18	31	28	0	3
Unit Outdating	100	2	59	90	68	0	0
Unit Holding	1,700	127	0	0	0	0	32
Unit Purchased	0	702	903	1,385	1,100	188	183
Fixed Cost	1.13	1.13	1.13	1.13	1.13	1.13	1.13
Average Cost/ Per Scenario	2,947	5,911	6,834	10,584	8,509	1,227	1,343

Table 4.14: Average Performance Measures for Hospital 2

	Hospital 2						
Performance Measure	**Monday**	**Tuesday**	**Wednesday**	**Thursday**	**Friday**	**Saturday**	**Sunday**
Unit Shortage	8	4	6	14	15	0	4
Unit Outdating	99	3	8	14	0	0	0
Unit Holding	1,700	115	66	70	108	59	95
Unit Purchased	0	801	892	1,357	993	190	155
Fixed Cost	2.25	2.25	2.25	2.25	2.25	2.25	2.25
Average Cost/ Per Scenario	3,127	5,517	6,150	9,446	7,100	1,314	1,277

Table 4.15: Average Performance Measures for Blood Center

	Blood Center						
Performance Measure	**Monday**	**Tuesday**	**Wednesday**	**Thursday**	**Friday**	**Saturday**	**Sunday**
Unit Shortage	0	0	0	0	0	0	0
Unit Outdating	0	0	0	0	0	0	0
Unit Holding	1,700	840	0	0	0	0	1,131
Unit Purchased	1,509	856	902	1,316	1,045	154	195
Fixed Cost	11.25	11.25	11.25	11.25	11.25	11.25	11.25
Average Cost/ Per Scenario	1,847	917	11.25	11.25	11.25	11.25	1,232

Table 4.16: Overall Performance Measures by Weekday

Overall Performance	**Monday**	**Tuesday**	**Wednesday**	**Thursday**	**Friday**	**Saturday**	**Sunday**
Average Cost/ Per Scenario	7,922	12,345	12,995	20,042	15,620	2,553	3,853
Best	6,267	10,623	11,754	17,838	13,723	2,472	3,255
Worst	16,095	19,616	17,922	27,653	24,864	2,862	5,724
STD	1,619	2,158	1,300	2,065	2,122	88	478

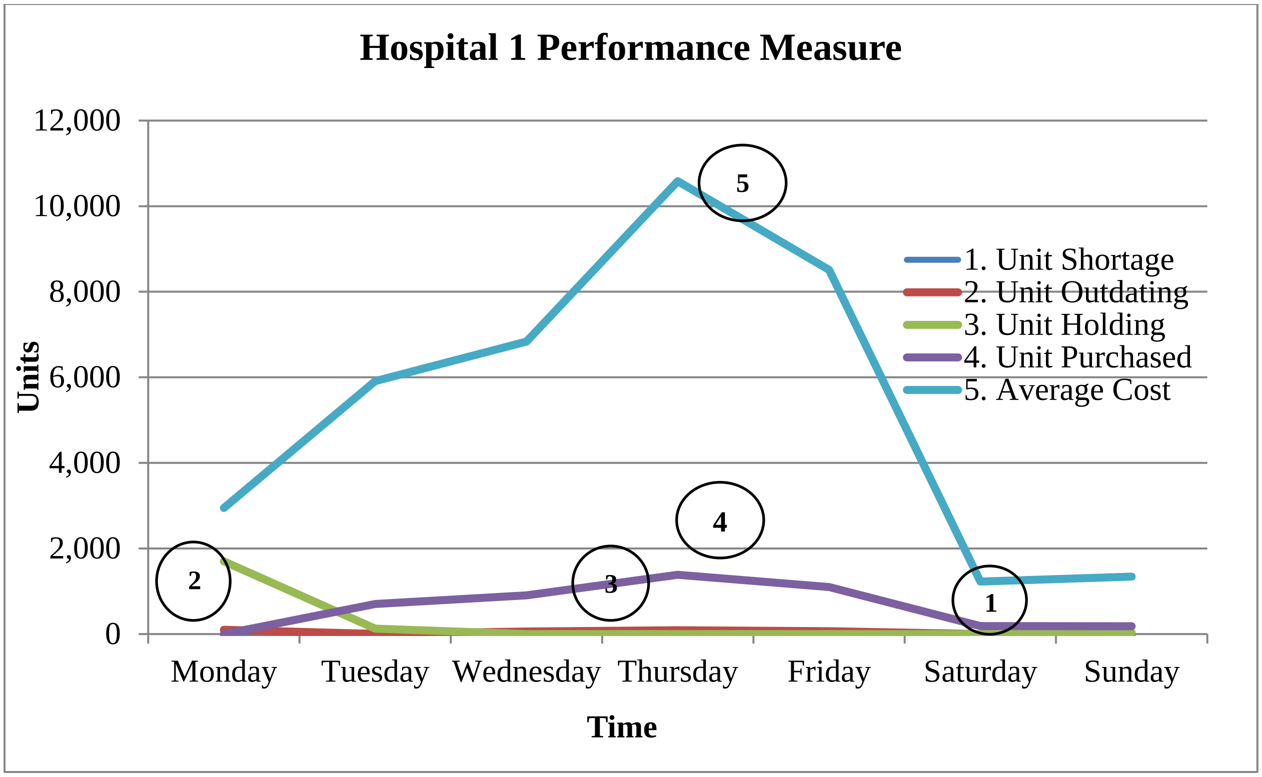


Figure 4.9: Performance Measures of Hospital 1 by Weekday

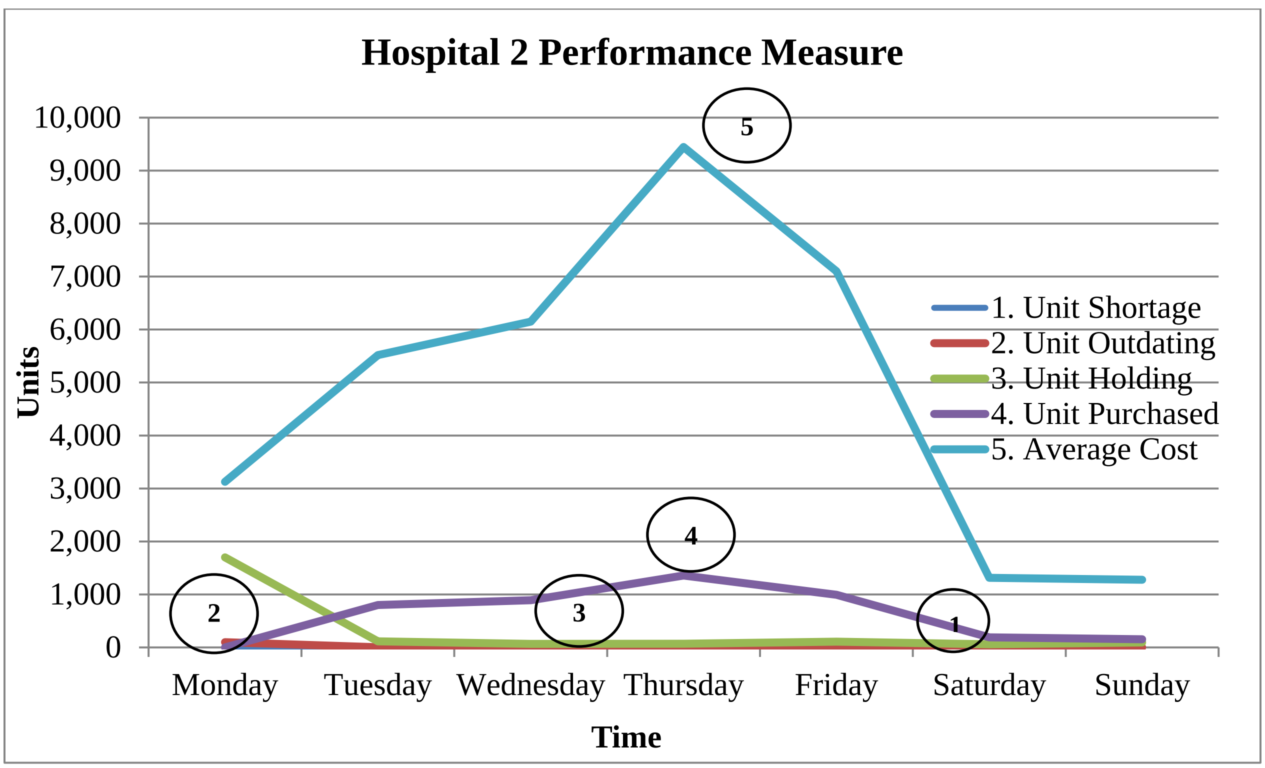


Figure 4.10: Performance Measures of Hospital 2 by Weekday

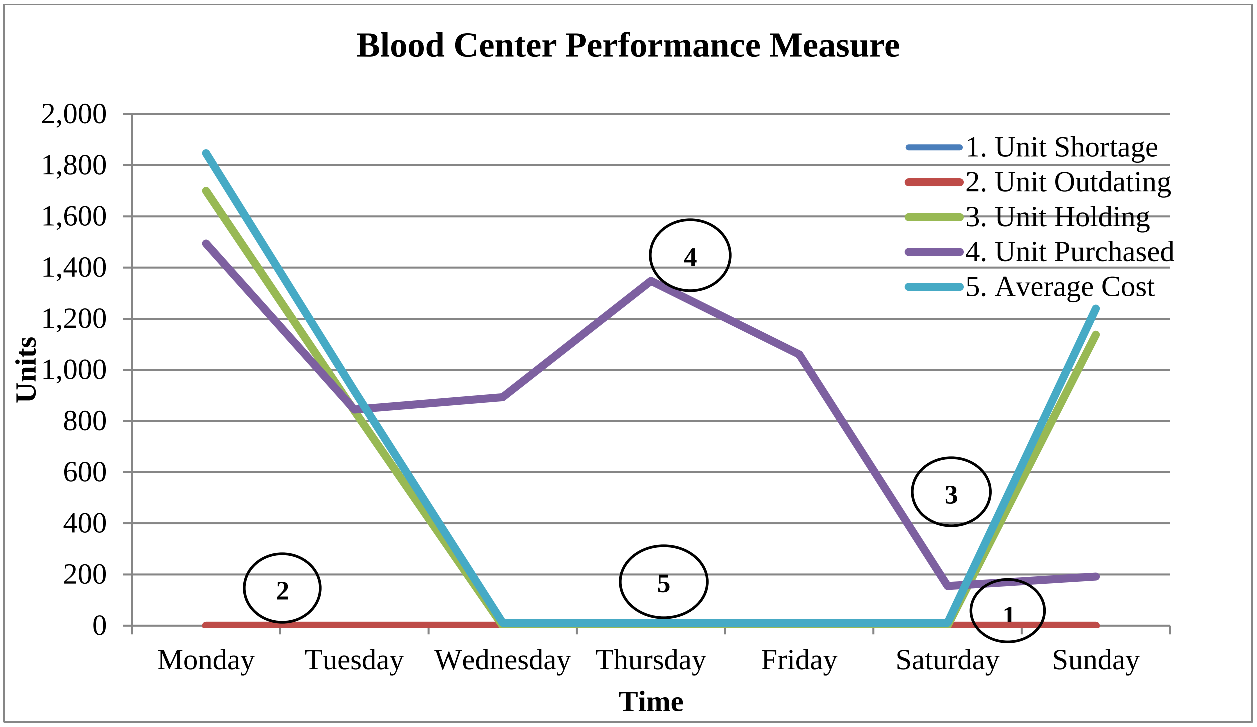


Figure 4.11: Performance Measures of Blood Center by Weekday

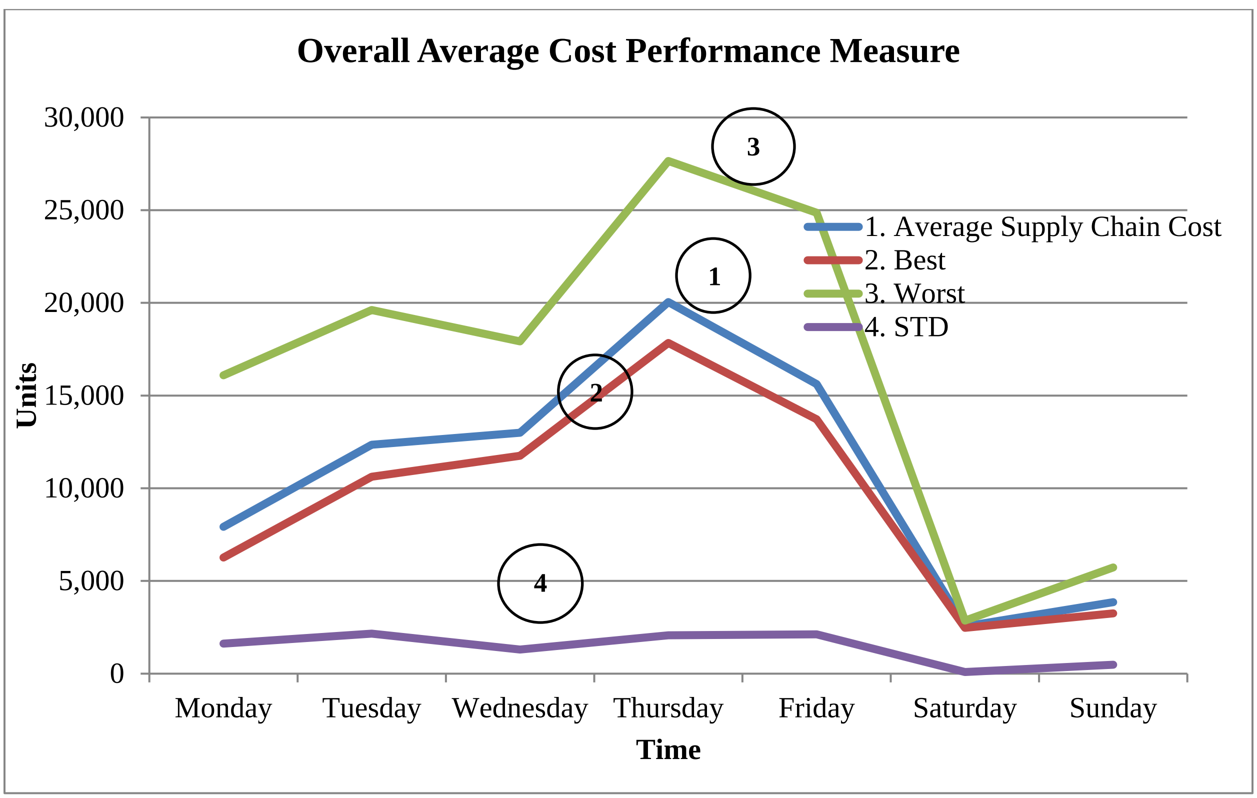


Figure 4.12: Overall Performance Measures of Supply Chain by Weekday

4.8 Implications of Results

The blood supply chain is genuinely unique as the products are very important to health care and life. Human blood cannot be manufactured, and no substitute for it has yet been successfully developed. Generally, many factors must be considered within the blood supply chain system because blood inventory management is a complex and challenging system. The collected donor blood faces a significant outdating because of the short shelf life of blood products. Moreover, hospitals and blood centers encounter serious blood inventory problems due to the uncertainty in blood demand and supply. In this study, we develop a stochastic mix integer linear programming model for the blood supply chain.

The problem with one blood center and two hospitals for a planning horizon frame of 300 days and 100 scenarios were solved to optimality using Python software with Gurobi Optimizer v8.1. It had 2,040,006 variables (90,000 are binary) and 1,621,202 constraints. It took about five minutes to process 417,279 iterations to solve the MILP problem. The results indicate that all the measures increase with the increase in the CV. This is because, with the increase in CV, more units are purchased to minimize shortage, which in turn results in more units held in inventory and more units expiring. It is also evident that settings with shortage and purchasing cost variations have the maximum deviation from the base case, while an insignificant change in total cost is observed for holding and outdating cost variation settings.

Even though more effort is required in the implementation of the mathematical model and the forecasts and generated supply an demand distributions have to be updated periodically, the model will result in less wastage and shortage. In practice, the same order policy may not be used for all the 300 days of the planning horizon. Instead, a rolling horizon approach may be followed to implement the optimal solution. For example, even though the MILP model gives an optimal order policy for 300 days, only the first week of the optimal solution is implemented. The case study implemented in this chapter focuses on weekday blood ordering for two hospitals and one blood center based on the assumption that the weekday demand and supply have the same normal distributions with various means. At the end of the first week, the MILP model is returned for the next 300 days after updating the inventory and demand distributions. The new optimal policy will be used for the second week, and the process is repeated weekly. Since long term forecasts may not be as good as short term forecasts, a rolling horizon policy helps to update forecasts weekly and determine the best solution decision based on the revised forecasts.

CHAPTER 5

PLATELET INVENTORY MANAGEMENT IN A DIVERGENT BLOOD SUPPLY CHAIN UNDER SUPPLY AND DEMAND UNCERTAINTY

5.1 Divergent Blood Supply Chain Model

While previous studies on blood supply chain management focus on a single blood center and a multi-hospital system, the objective of the current study is to determine the optimal ordering policy for a divergent network consisting of multiple blood centers and hospitals. To achieve this goal, a stochastic mixed integer programming model is developed to minimize the total supply chain cost (consisting of transportation, purchasing, shortage, outdating, and inventory costs) in the healthcare network. Sensitivity analysis is conducted to investigate the influence of the supply and demand variation, as well as the cost parameters on the performance measures, such as shortage, outdating, holding, units purchased, and total cost.

5.1.1 System Description

The blood supply chain framework examined in this study consists of X blood centers and K hospitals (as shown in Figure 5.1). Each blood center can ship platelets to any of the K hospitals. The cost of transporting platelets will depend on the distance between the blood center and hospital. Current Health Insurance Portability and Accountability Act (HIPAA) regulations strongly discourage the exchange of blood among hospitals due to traceability issues. Therefore, in this research, we assume that hospitals can receive platelets only from blood center and are not allowed to share blood among each other. A collaborative system of blood centers and hospitals is better than a decentralized system in which each hospital is supplied with blood only by its corresponding blood center, as proven in the APPENDIX.

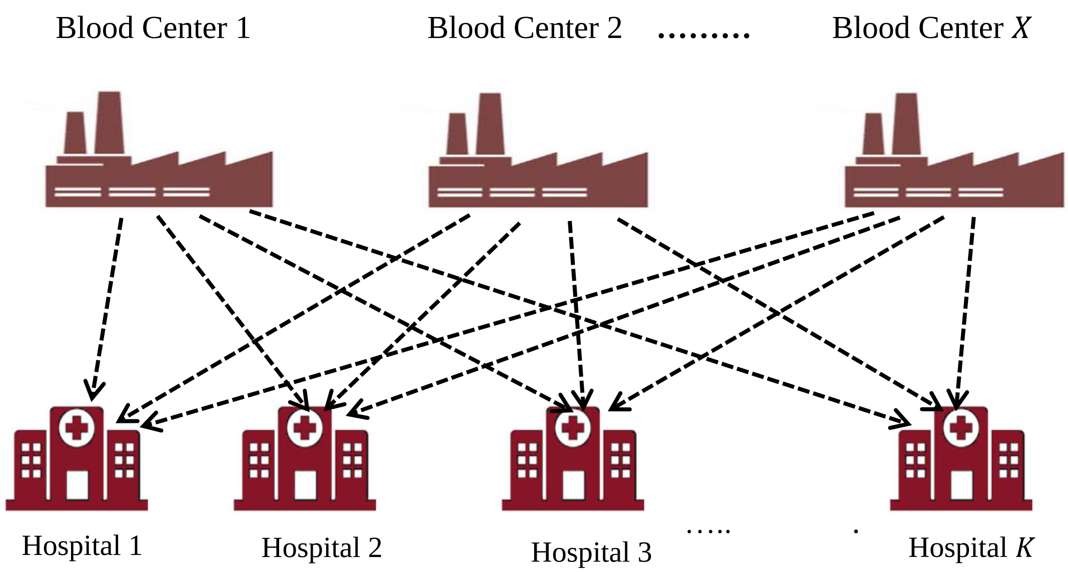


Figure 5.1: Structure of Supply Chain Containing X Blood Centers and K Hospitals

5.2 Methodology

This section describes the stochastic mixed integer linear programming (MILP) model utilized in this study. We use the scenario-based approach, in which each scenario is derived from a unique set of demand and supply patterns. Under this approach, the number of units purchased through the regular procurement remains unchanged, whereas the amount of units obtained during any emergency, units inventory, expiration and shortage varies depending on the scenario.

5.2.1 Model Assumptions:

1. Order processing lead time is negligible
2. Only one blood type is considered in the model
3. The hospital utilizes FIFO policy, which means that for demand fulfillment, the units with one-day shelf life are used first, followed by two days and then three days shelf life.

5.2.2 Notations for the Model

<u>Model parameters (known data)</u>

l	Index of platelets shelf life (l =1,2,3)
k	Index of hospital k

x	Index of blood center x
s	Index of demand scenario (demand patterns for platelet) (s =1, 2, …, S)
t	Index of day t (t =1, 2, …, T)
K	Total number of hospitals (k =1, 2, …, K)
X	Total number of blood centers (x =1, 2, …, X)
$pb(s)$	Probability of scenario s ($\sum_1^S pb(s) = 1$)
$foHP_k$	Fixed operational cost per day at hospital k ($/day)
$fsHP_{x,k}$	Fixed shipping charges for procuring platelets at hospital k from blood center x ($/shipment) ($x$ =1, 2, …, X)
$pcHP$	Purchasing cost for each unit of platelet at hospital ($/unit)
$hcHP$	Platelet inventory holding cost per unit per day at hospital ($/day/unit)
$ecHP$	Cost of expired platelet per unit at hospital ($/unit)
$scHP$	Shortage cost per unit at hospital ($/unit) (this is the purchasing cost incurred per platelet unit due to the shipment from the blood center during an emergency)
$demand_{k,t}(s)$	Platelet demand at hospital k on day t (units) under scenario s. Historical data is leveraged to estimate the demand
$ltHP_{x,k}$	Lead time (days) of procurement at hospital k from blood center x. It is the time between issuing orders for platelets and receiving them (Note: $ltHP_{x,k}$ = 0,1 or 2 only)
$rpHP_k$	Order review period at hospital k (days)
$iniHP_{k,l}$	Beginning inventory at hospital k on day 1 with l days shelf life
$fsBC_x$	Fixed shipping charges for procuring platelets incurred by blood center ($/shipment) ($x$ =1, 2, …, X)
$hcBC$	Platelet inventory holding cost per unit per day associated with the blood center ($/day)
$ecBC$	Platelet outdating cost per unit related to the blood center ($/unit)
$scBC$	Shortage cost per unit ($/unit) related with the blood center (this is referring to the purchasing cost per unit of platelets due to shipment from blood centers during an emergency from other blood centers)

$supply_{x,t}(s)$	Number of units of platelet supply at blood center x on day t under scenario s. Historical data is used to estimate supply pattern (x =1, 2, …, X)
$ltBC_x$	Lead time in days to purchase platelets for blood center x. It is the time between issuing orders and receiving fresh new platelets. It comprises of the total time for collecting as well as two days of testing time (x =1, 2, …, X)
$rpBC_x$	The review period for platelets ordering at the blood center x (days) (x =1, 2,…, X)
$iniBC_{x,l}$	Starting inventory at blood center x on day one with a shelf life of l days (x = 1, 2, …, X)

Key Decision Variables for the Model

$ORHP_{k,t}(s)$	The number of units ordered by hospital k to the blood centers at the end of the day t in scenario s
$REHP_{k,t,l}(s)$	The number of units procured by hospital k at the beginning of day t from all the X blood centers having a shelf life of l days (l =1,2,3), in scenario s (note: the incoming platelets units have a maximum storage life of three days)
$OHHP_{k,t,l}(s)$	Existing platelet inventory having a shelf life of l days (l =1, 2) at the beginning of day t, at hospital k, in scenario s. Note: The available inventory can have a maximum shelf life of two days at the start of day t. This is because the maximum shelf life of the platelet units is three days
$SHHP_{k,t}(s)$	The number of platelet unit shortage at hospital k by the end of day t, at hospital k, in scenario s (note: Hospital k obtains these shortage units via emergency shipments from the blood center)
$EXHP_{k,t}(s)$	The number of units that are expired at hospital k at the end of day t, in scenario s

Key Decision Variables regarding Blood Centers in the Model

$ORBC_{x,t}(s)$	The number of units ordered by blood center x at the end of day t in scenario s. These units will be received by the blood center x at the beginning of day $t + LTBC_x$ after the component labs finish the testing process
$REBC_{x,t}(s)$	The number of units received by blood center x from the component labs at the beginning of day t, after finishing the testing process in scenario s (note: The units procured by the blood center will be fresh and have a shelf life of three days)

$BCTHP_{x,k,t,l}(s)$	On day t, the number of units shipped to hospital k with platelets having a shelf life of l days (l =1,2,3) from the blood center x, in scenario s
$OHBC_{x,t,l}(s)$	The number of on-hand units with a shelf life of l days (l =1, 2) at the beginning of day t, at blood center x, in scenario s. Note: Since the maximum shelf life at the start of day t is three days, the carried inventory (brought over from day t −1) can only have a maximum of two days of shelf life
$SHBC_{x,t}(s)$	The number of shortage units at the blood center x in scenario s at the end of day t
$EXBC_{x,t}(s)$	The number of platelet units that are expired at the blood center x in scenario s at the end of day t

Objective Function for the Model

$TCSC$ Estimated total cost collected for all possible scenarios through the finite time period (T) in the blood supply chain

5.3 Blood Supply Chain Model Formulation

The objective function is to minimize the total cost incurred by the entire blood supply chain. The objective function considers nine different cost components affiliated with the entire supply chain:

- The cost associated with hospital k, blood center x on day t:
  - Fixed transportation cost: $fsHP_{x,k} \times binHP_{k,t}(s)$
  - Variable purchasing cost: $pcHP \times ORHP_{k,t}(s)$
  - Inventory holding cost: $hcHP \times \left(OHHP_{k,t,1}(s) + OHHP_{k,t,2}(s)\right)$
  - Shortage cost: $scHP \times SHHP_{k,t}(s)$
  - Expiration cost: $ecHP \times EXHP_{k,t}(s)$
- The cost related to the blood center x on day t:
  - Fixed transportation cost: $fsBC_x \times binBC_{x,t}(s)$
  - Inventory holding cost: $hcBC \times \left(OHBC_{x,t,1}(s) + OHBC_{x,t,2}(s)\right)$
  - Shortage cost: $scBC \times SHBC_{x,t}(s)$
  - Expiration cost: $ecBC \times EXBC_{x,t}(s)$

Note: Cost for processing and testing blood platelets at blood centers are not taken into account in the current objective function as they are included under procurement costs charged to the hospitals. To minimize the expected total cost across all scenarios over the entire blood supply chain under demand and supply uncertainty, the objective function is formulated as follows:

Minimize $TCSC =$

$$\sum_{t=1}^{T}\Big[\sum_{s=1}^{S}\Big[pb(s)\times\Big\{\sum_{k=1}^{K}\Big[\sum_{x=1}^{X}[fsHP_{x,k}\times binHP_{k,t}(s)+\ pcHP\times ORHP_{k,t}(s)]+hcHP\times \Big(OHHP_{k,t,1}(s)+OHHP_{k,t,2}(s)\Big)+scHP\times SHHP_{k,t}(s)+ecHP\times\ EXHP_{k,t}(s)\Big]+ \sum_{x=1}^{X}[fsBC_{x}\times binBC_{x,t}(s)+hcBC\times\Big(OHBC_{x,t,1}(w)+OHBC_{x,t,2}(s)\Big)+scBC\times SHBC_{x,t}(s)+ ecBC\times EXBC_{x,t}(s)]\Big\}\Big]\Big] \quad (5.1)$$

$REHP_{k,t,l}(s)=\sum_{x=1}^{X}BCTHP_{x,k,t-ltHP_{x,k},l+ltHP_{x,k}}(s)$ $\quad \forall x,t>ltHP_{x,k}$ and $l+ltHP_{x,k}\leq 3$ (5.2)

$REHP_{k,t,l}(s)=0$ Otherwise (5.3)

$$demand_{k,t}(s)-OHHP_{k,t,1}(s)-REHP_{k,t,1}(s) = RDHP_{k,t,1}(s)-LYHP_{k,t,1}(s) \quad \forall\ k,t,s \quad (5.4)$$

$$RDHP_{k,t,1}(s)-OHHP_{k,t,2}(s)-REHP_{k,t,2}(s) = RDHP_{k,t,2}(s)-LYHP_{k,t,2}(s) \quad \forall\ k,t,s \quad (5.5)$$

$$RDHP_{k,t,2}(s)-REHP_{k,t,3}(s)=RDHP_{k,t,3}(s)-LYHP_{k,t,3}(s) \quad \forall\ k,t,s \quad (5.6)$$

$$EXHP_{k,t}(s)=LYHP_{k,t,1}(s) \quad \forall\ k,t,s \quad (5.7)$$

$$OHHP_{k,t+1,1}(s)=LYHP_{k,t,2}(s) \quad \forall\ k,t,s \quad (5.8)$$

$$OHHP_{k,t+1,2}(s)=LYHP_{k,t,3}(s) \quad \forall\ k,t,s \quad (5.9)$$

$$SHHP_{k,t}(s)=RDHP_{k,t,3}(s) \quad \forall\ k,t,s \quad (5.10)$$

$$OHHP_{k,1,l}(s)=iniHP_{k,l} \quad \forall\ k,l,s \quad (5.11)$$

$$ORHP_{k,t,l}(s)=0 \quad \forall\ k,t\neq rpHP_{k},2rpHP_{k},\dots,l,s \quad (5.12)$$

$$ORBC_{x,t}(s)=0 \quad \forall\ x,t\neq rpBC_{x},2rpBC_{x},\dots,s \quad (5.13)$$

$$REBC_{x,t}(s)=ORBC_{x,t-ltBC_{x}}(s) \quad \forall\ x,t>ltBC_{x},s \quad (5.14)$$

$$ORBC_{x,t}(s)=SUPPLY_{x,t}(s) \quad \forall\ x,t,s \quad (5.15)$$

$$\sum_{k=1}^{K}BCTHP_{x,k,t,1}(s)+LFRBC_{x,t,1}(s)=OHBC_{x,t,1}(s) \quad \forall\ x,t,s,ltHP_{x,k}=0 \quad (5.16)$$

$$\sum_{k=1}^{K}BCTHP_{x,k,t,2}(s)+LFRBC_{x,t,2}(s)=OHBC_{x,t,2}(s)\ \forall\ x,t,s,ltHP_{x,k}=0{,}1 \quad (5.17)$$

(In general, $\sum_{k=1}^{K} BCTHP_{x,k,t,l}(s) + LFRBC_{x,t,l}(s) = OHBC_{x,t,l}(s)\ \forall\ x, t, s, and\ l = 1{,}2, ltHP_{x,k} \leq l$)

$$\sum_k HP3_{k,t}(s) + \sum_{x=1}^{X} LFRBC_{x,t,3}(s) = \sum_{x=1}^{X} REBC_{x,t}(s) \quad \forall\ t, s, ltHP_{x,k} = 0{,}1{,}2 \tag{5.18}$$

$$\sum_{x=1}^{X}\left[BCTHP_{x,k,t,1}(s) + BCTHP_{x,k,t,2}(s)\right] + HP3_{k,t}(s) + \sum_{x=1}^{X} SHRBC_{x,k,t}(s) = ORHP_{k,t}(s) \quad \forall\ t, k, s \tag{5.19}$$

$$\sum_{x=1}^{X} BCTHP_{x,k,t,3}(s) = HP3_{k,t}(s) + \sum_{x=1}^{X} SHRBC_{x,k,t}(s) \quad \forall\ t, k, s \tag{5.20}$$

$$\sum_k SHHP_{k,t}(s) - \sum_{x=1}^{X} LFRBC_{x,t,1}(s) = \sum_{x=1}^{X} RSHBC_{x,t,1}(s) - \sum_{x=1}^{X} LFEBC_{x,t,1}(s) \quad \forall\ t, s \tag{5.21}$$

$$RSHBC_{x,t,1}(s) - LFRBC_{x,t,2}(s) = RSHBC_{x,t,2}(s) - LFEBC_{x,t,2}(s) \quad \forall\ x, t, s \tag{5.22}$$

$$RSHBC_{x,t,2}(s) - LFRBC_{x,t,3}(s) = RSHBC_{x,t,3}(s) - LFEBC_{x,t,3}(s) \quad \forall\ x, t, s \tag{5.23}$$

$$SHEBC_{x,t}(s) = RSHBC_{x,t,3}(s) \quad \forall\ x, t, s \tag{5.24}$$

$$EXBC_{x,t}(s) = LFEBC_{x,t,1}(s) \quad \forall\ x, t, s \tag{5.25}$$

$$OHBC_{x,t+1,1}(s) = LFEBC_{x,t,2}(s) \quad \forall\ x, t, s \tag{5.26}$$

$$OHBC_{x,t+1,2}(s) = LFEBC_{x,t,3}(s) \quad \forall\ x, t, s \tag{5.27}$$

$$SHBC_{x,t}(s) = \sum_k SHRBC_{x,k,t}(s) + SHEBC_{x,t}(s) \quad \forall\ x, t, s \tag{5.28}$$

$$OHBC_{x,1,l}(s) = iniBC_{x,l} \quad \forall\ x, l, s \tag{5.29}$$

$$REHP_{k,t,l}(1) = REHP_{k,t,l}(2) = \cdots = REHP_{k,t,l}(s) \quad \forall\ k, t, l, s \tag{5.30}$$

$$ORHP_{k,t,l}(1) = ORHP_{k,t,l}(2) = \cdots = ORHP_{k,t,l}(s) \quad \forall\ k, t, l, s \tag{5.31}$$

$$REHP_{k,t,1}(s) + REHP_{k,t,2}(s) + REHP_{k,t,3}(s) \leq M \times binHP_{k,t}(s) \quad \forall\ k, t, s \tag{5.32}$$

$$REBC_{x_t}(s) \leq M \times binBC_{x,t}(s) \quad \forall\ x, t, s \tag{5.33}$$

$$SHHP_{k,t}(s), EXHP_{k,t}(s), LFRBC_{x,k,t,l}(s), BCTHP_{x,k,t,l}(s), HP3_{k,t}(s), REBC_{x,t}(s), SHRBC_{x.k,t}(s), LFEBC_{x,t,l}(s), OHBC_{x,t,l}(s), LBC_{x,t}(s), ORBC_{x,t}(s), SHEBC_{x,t}(s), SHBC_{x,t}(s), EXBC_{x,t}(s), RSHBC_{x,t}(s) \geq 0 \quad \forall\ x, l, k, t, s \tag{5.34}$$

$$binHP_{k,t}(s) \in \{0{,}1\} \quad \forall\ k, t, s \tag{5.35}$$

$$binBC_{x,t}(s) \in \{0{,}1\} \quad \forall\ x, t, s \tag{5.36}$$

Units of Platelet Obtained by the Hospital k from the Blood Center

The total number of units received by hospital k from blood center x having a life of l days ($REHP_{k,t,l}(s)$), will be equal to the number of components delivered from blood center x on day $t - ltHP_{x,k}$, having a shelf life of $l + ltHP_{x,k}$ days as shown by Equation (5.2). (Note: $ltHP_{x,k}$ = 0, 1 or 2 days).

Uncertainty Demand-Inventory Balance at Hospital k and Day t under Scenario s

Equation (5.4) describes that if the number of platelet units having a shelf life of just one day is less than the stochastic demand at hospital k (i.e., $OHHP_{k,t,1}(s) + REHP_{k,t,1}(s) < demand_{k,t}(s)$), then the remaining inventory having a single day shelf life ($LYHP_{k,t,1}(s)$) is equal to zero, and the residual demand ($RDHP_{k,t,1}(s)$) is computed as $demand_{k,t}(s) - OHHP_{k,t,1}(s) - REHP_{k,t,1}(s)$. However, if the reverse is true (i.e., $OHHP_{k,t,1}(s) + REHP_{k,t,1}(s) \geq demand_{k,t}(s)$) then leftover inventory is computed as $LYHP_{k,t,1}(s) = OHHP_{k,t,1}(s) + REHP_{k,t,1}(s) - demand_{k,t}(s)$ and $RDHP_{k,t,1}(s) = 0$.

If the remaining demand ($RDHP_{k,t,1}(s)$) is greater than zero, then it is fulfilled by the units having a shelf life of two days ($OHHP_{k,t,2}(s) + REHP_{k,t,2}(s)$). Suppose $RDHP_{k,t,1}(s) > OHHP_{k,t,2}(s) + REHP_{k,t,2}(s)$, then remaining demand $RDHP_{k,t,2}(s)$ is estimated as $RDHP_{k,t,1}(s) - OHHP_{k,t,2}(s) - REHP_{k,t,2}(s)$ and the reserve having a two-day life ($LYHP_{k,t,2}(s)$) will be zero. Likewise, if $RDHP_{k,t,1}(s) \leq OHHP_{k,t,2}(s) + REHP_{k,t,2}(s)$, the surplus platelets with a shelf life of two days is calculated by $LYHP_{k,t,2}(s) = OHHP_{k,t,2}(s) + REHP_{k,t,2}(s) - RDHP_{k,t,1}(s)$ and $RDHP_{k,t,2}(s)$ = 0. Parameters $RDHP_{k,t,2}(s)$ and $LYHP_{k,t,2}(s)$ are computed by Equation (5.5).

Similarly, if $RDHP_{k,t,2}(s)$ is greater than zero, then platelets having three day longevity ($REHP_{k,t,3}(s)$) is used to satisfy the remaining demand ($RDHP_{k,t,2}(s)$). If $RDHP_{k,t,2}(s) > REHP_{k,t,3}(s)$, then the rest of the demand ($RDHP_{k,t,3}(s)$) is determined by $RDHP_{k,t,2}(s) - REHP_{k,t,3}(s)$ and the remaining units with three-day life $LYHP_{k,t,3}(s)$ is equal to zero. However, if $RDHP_{k,t,2}(s) \leq REHP_{k,t,3}(s)$, then the residual stocks with a shelf life of three days is estimated by $LYHP_{k,t,3}(s) = REHP_{k,t,3}(s) - RDHP_{k,t,2}(s)$ and $RDHP_{k,t,3}(s) = 0$. The two Parameters $RDHP_{k,t,3}(s)$ and $LYHP_{k,t,3}(s)$ are computed by Equation (5.6).

Equation (5.7) identifies that the unused platelet units that have a life of just one day ($LYHP_{k,t,1}(s)$) are discarded by hospital k at the end of day t. Constraints (5.8) and (5.9) depicts that the record of the stockpile at hospital j are amended every day at the close. It should be noted that each hospital has a distinct inventory, which is dependent on the supply and demand scenario. Equation (5.10) gives the unfulfilled demand, $RDHP_{k,t,3}(s)$ which is equivalent to the amount of platelet scarcity at the end of any day ($SHHP_{k,t}(s)$). The starting inventory in hospital k at time t = 1 for a scenario s is estimated using Constraint (5.11).

Platelets can only be ordered by a hospital k during review periods ($t = RPHP_k, 2RPHP_k, \ldots$) and orders cannot be scheduled on other days. This is described by Equation (5.12). Constraint (5.13) is comparable with Equation (5.12), where the blood center x can only place orders for platelet units during review periods ($t = RPBC_x, 2RPBC_x, \ldots$), and cannot request orders during other days. Once the comprehensive testing is concluded at the blood center x, the number of units accessible at the beginning of day t for any scenario s ($REBC_{x,t}(s)$) is estimated through Constraints (5.14) and (5.15), which is the amount ordered before lead time ($ORBC_{x,t-LTBC_x}(s)$). Existing supply data is utilized to calculate the quantity required by blood center x at the start of each day t for any scenario s, as shown by Equation (5.15).

Fulfillment for the Regular Platelet Demand by the Blood Center

The policy required to satisfy the hospital demand is evaluated by the model using Equations (5.16) – (5.18). The total platelet units (dependent on lead time) distributed to hospital k from blood center x having l days of life on day t ($BCTHP_{x,k,t,l}(s)$) id the decision variables in the above equations. Constraints (5.16) and (5.17) ensure that the blood center supplies units having at least two days shelf life if the hospital k has a lead time of one day because in such scenarios the platelets would expire upon arrival. Similarly, if the lead time of the platelet units is two days, then the preservation life of blood supplied to the medical center should be three days as described by Equation (5.18). Also, a lead time of zero days would mean that the blood center can ship the units with life of any day as given by Constraint (5.16) – (5.18). Any shortage experienced by blood center x ($SHRBC_{x,k,t}(s)$) is estimated using Constraint (5.19). The units required to fulfill the demand at hospital k would be procured from other blood facilities. It is assumed in the model that the acquired units would have a shelf life of three days. Equation (5.20) shows that $\sum_{x=1}^{X} SHRBC_{x,k,t}(s)$ from blood center x should be integrated with $HP3_{k,t}(s)$ where $HP3_{k,t}(s)$ is the available inventory at hospital k having a shelf life of three days.

Fulfillment for the Emergency Demand by the Blood Center

Once the regular demand at medical facility k is fulfilled (i.e., $\sum_k SHHP_{k,t}(s)$ is satisfied with $\sum_{x=1}^{X} \sum_l LFRBC_{x,t,l}(s)$) the emergency demand will be realized only via inventory, as discussed by Equations (5.21) – (5.23) through blood center x. $LFEBC_{x,t,l}(s)(l = 1,2,3)$ at blood center x in Constraints (5.21) – (5.23) depicts the surplus quantity of platelet units having a life of one day, two days, or three days after completing the emergency demand. $RSHBC_{x,t,l}(s)(l = 1,2,3)$ at blood center x is the required amount to be achieved. Therefore, based on the demand for emergency units, Equation (5.24) computes the total shortage of platelets at the blood facility.

The total number of platelet units that are expired and remaining inventory after the end of day t at facility X are given by Equations (5.25) and (5.26) - (5.27), respectively. The insufficient quantity of platelets under scenario s is given by the summation of regular (($\sum_k SHRBC_{x,k,t}(s)$) and emergency demand ($SHEBC_{x,t}(s)$), as shown in Constraint (5.28). The starting inventory at blood center x at time $t = 1$ in scenario s is presented by Equation (5.29). The number of units obtained and ordered by hospital k is identical for all situations across the entire supply chain, as described by constraints (5.30) and (5.31), respectively. The total quantity of platelets acquired by the medical center k having a life of l days at the beginning of day t is defined by Constraint (5.32). On the other hand, the total amount of units distributed to blood center x from testing labs at the start of day t for case s is indicated by Equation (5.33). Constraint (5.34) ensures that the equations have non-negative integer values. Likewise, Constraints (5.35) – (5.36) gives the non-negative binary equations for the model.

5.4 Computational Results

For the purpose of illustrating the proposed model, we consider two blood centers and four hospitals. It is assumed that hospitals #1 and #2 are in close proximity to blood center #1 and are located away from blood center #2. Whereas hospitals #3 and #4 are closer to blood center #2, however, they are situated relatively far away from blood center #1.

The stochastic model for the blood supply chain is programmed in Python® and solved using the Gurobi Optimizer v8.1. The problem is composed of two blood centers and four hospitals and it has 1,822,173 variables (100,000 are binary) and 1,803,208 constraints. The processing time for a planning horizon of 100 days and 100 scenarios with 531,677 iterations is about one hour and 30 minutes. Sensitivity analysis is conducted to analyze the performance of the model by altering the coefficient of supply and demand variation.

5.4.1 Base Case Results

The input parameters for the base case setting obtained from the literature (Haijema, 2013; Civelek et al., 2015; Rajendran and Ravindran, 2017; Rajendran and Ravindran, 2019) are presented in Table 5.1. The average performance measure for the baseline model, along with the overall cost is given in Table 5.2.

We can observe that for hospital 1, more units are purchased from the blood center, which in turn results in more platelets being held in inventory leading to more outdating. In contrast, hospital 2 procures the least amount of units and thus has the lowest inventory level. Hospitals 3 and 4 have about the same amount of units purchased, leading to a similar unit holding and outdating.

Table 5.1: Input Parameters for the Baseline Setting

Base Case	Hospital				Blood Center	
	#1	#2	#3	#4	#1	#2
Lead Time from BC 1 (days)	0	0	1	1	-	-
Lead Time from BC 2 (days)	1	1	0	0	-	-
Review Period (days)	1					
Inventory Cost ($/day/unit)	130				108	
Outdating Cost ($/unit)	650				538	
Shortage Cost ($/unit)	3,250				2,690	
Variable Purchasing Cost ($/unit)	650				-	
Fixed Ordering Cost from BC 1 ($/shipment)	113	225	339	675	-	-
Fixed Ordering Cost from BC 2 ($/shipment)	339	675	113	225	-	-
Demand/Supply Distribution	N ~ (150, 24)	N ~ (50, 8)	N ~ (100, 16)	N ~ (100, 16)	N ~ (225, 37)	N ~ (225, 37)

Table 5.2: Average Performance Measure for the Baseline Setting

Performance Measure per Day per Scenario	Hospital				Blood Center	
	#1	#2	#3	#4	#1	#2
Unit Shortage	1	0	0	0	1	0
Unit Outdating	4	1	2	3	36	0
Unit Holding	31	11	21	21	3	73
Unit Purchased	155	51	103	104	225	225
Fixed Ordering Cost from Blood Centers	167	371	137	415	-	-
Overall Measure						
Average Total Supply Chain Cost	Best		Worst		STD	
3,253	3,168		3,375		40	

5.5 Sensitivity Analysis

The impact of variation in the demand and supply, along with cost settings on numerous factors, such as units purchased, shortage, holding, outdated, and total cost is investigated in this section.

5.5.1 Variation in the Mean Demand

Various demand settings (DS) utilized in the model are shown in Table 5.3. For each scenario, the mean demand is increased or decreased by a factor of 0.25 for a particular medical facility while keeping the other values constant. For example, for demand setting 2, the mean value for hospital #1 is multiplied by 1.25 while retaining the same demand for other health centers. Similarly, for demand setting 3, the mean value for hospital #1 is multiplied by 0.75 while maintaining the consistent demand for other health facilities. Likewise, the demand is varied for hospital #2 in DS4 and 5, for hospital #3 in DS6 and 7, and for hospital #4 in DS8 and 9.

It is observed that all hospitals, in general, have an unsubstantial amount of shortage and outdated units. This is due to the negligible lead time from the blood centers. On the other hand, blood center #1 has a higher volume of outdated units when compared to blood center #2, although both centers follow the same supply distribution. This may be because the demand variation at hospitals associated with the former (i.e., hospitals #1 and #2) have higher variation in demand compared to those that are affiliated with blood center #2. It is noticed that hospital #2 purchases less than half the quantity of platelets when compared to other hospitals, which results in fewer units in the inventory, as well as less outdating. Figure 5.2(a) – (f) displays the effect of various demand settings on the multiple performance measures of the blood supply chain.

Table 5.4 presents the overall cost measure for various demand settings. Demand setting 3 displayed the lowest average cost per day per scenario. Also, DS5, 7 and 9 showcase a lower cost value when compared to the base case setting. On the other hand, DS2 exhibits the highest average cost per day per scenario because of having the highest number of total units in the system.

Table 5.3: Various Demand Settings Considered in the Present Study

Setting	Hospital 1		Hospital 2		Hospital 3		Hospital 4		Blood Center 1		Blood Center 2	
	Mean	**STD**	**Mean**	**STD**	**Mean**	**STD**	**Mean**	**STD**	**Mean**	**STD**	**Mean**	**STD**
DS1 (base)	150	24	50	8	100	16	100	16	225	37	225	37
DS2	**188**	**24**	50	8	100	16	100	16	225	37	225	37
DS3	**113**	**24**	50	8	100	16	100	16	225	37	225	37
DS4	150	24	**63**	**8**	100	16	100	16	225	37	225	37
DS5	150	24	**38**	**8**	100	16	100	16	225	37	225	37
DS6	150	24	50	8	**125**	**16**	100	16	225	37	225	37
DS7	150	24	50	8	**75**	**16**	100	16	225	37	225	37
DS8	150	24	50	8	100	16	**125**	**16**	225	37	225	37
DS9	150	25	50	9	100	17	**75**	**16**	225	37	225	37

Table 5.4: Overall Cost Measure for Various Demand Settings

Setting	Average Cost per Day per Scenario (Best, Worst, STD)
DS1 (base)	3,253 (3,168, 3,375, 40)
DS2	3,508 (3,359, 3,788, 78)
DS3	3,127 (3,052, 3,222, 32)
DS4	3,312 (3,200, 3,433, 51)
DS5	3,202 (3,105, 3,313, 41)
DS6	3,370 (3,237, 3,532, 52)
DS7	3,163 (3,073, 3,260, 42)
DS8	3,385 (3,264, 3,571, 50)
DS9	3,180 (3,093, 3,326, 40)

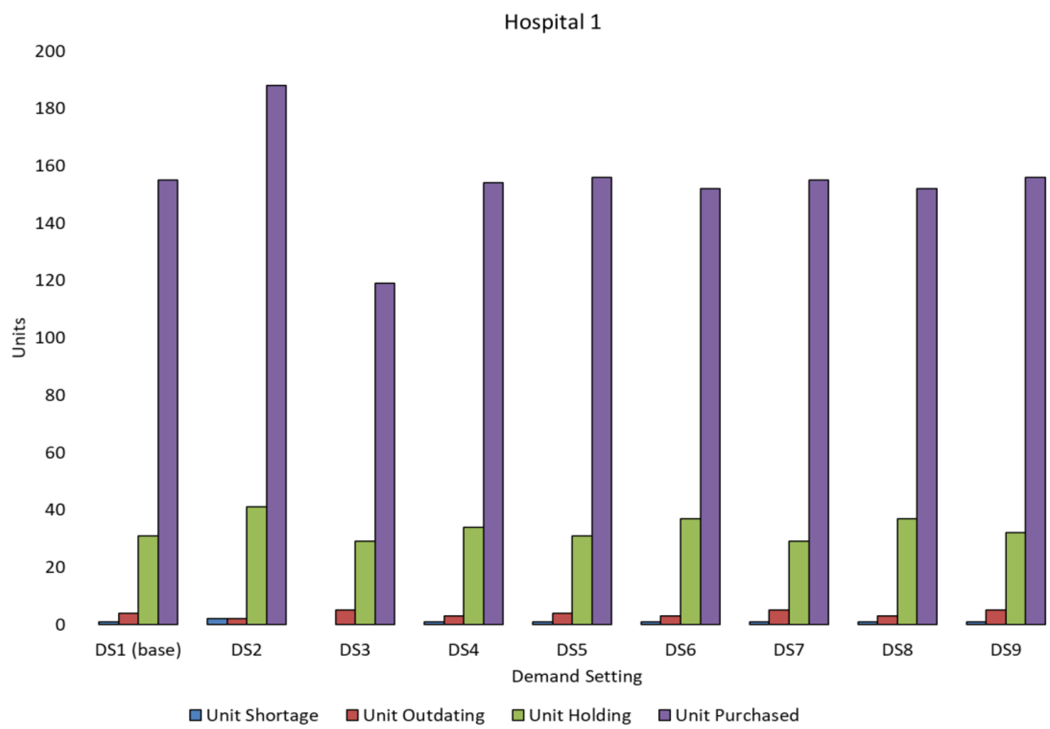


Figure 5.2(a)

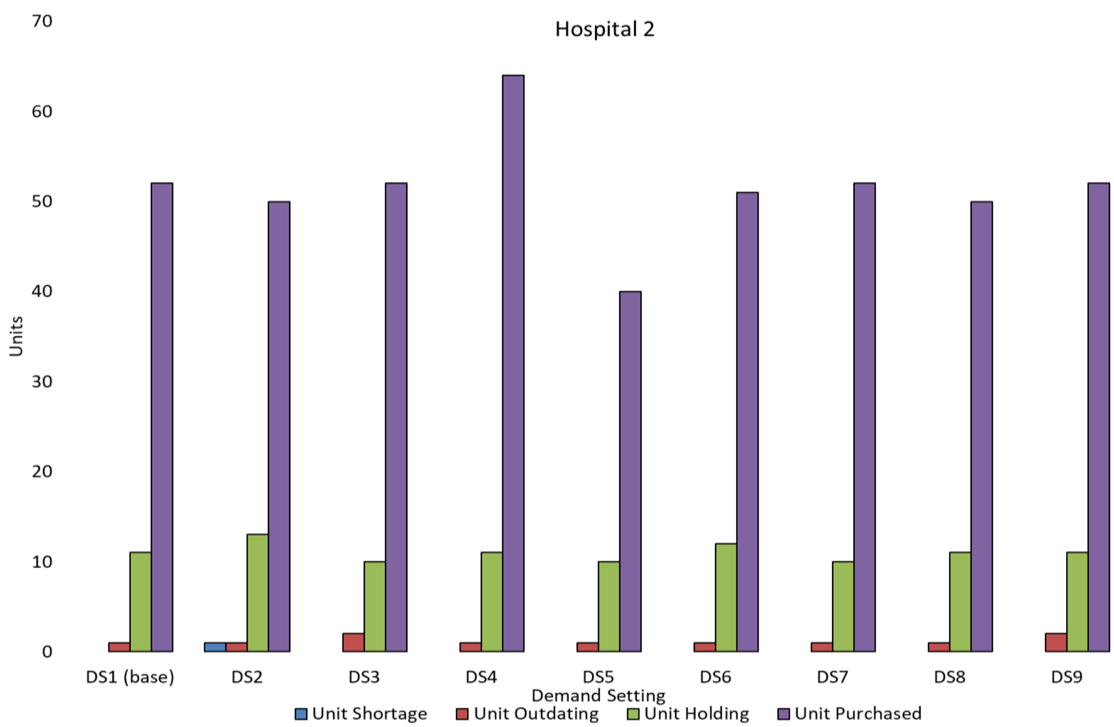


Figure 5.2(b)

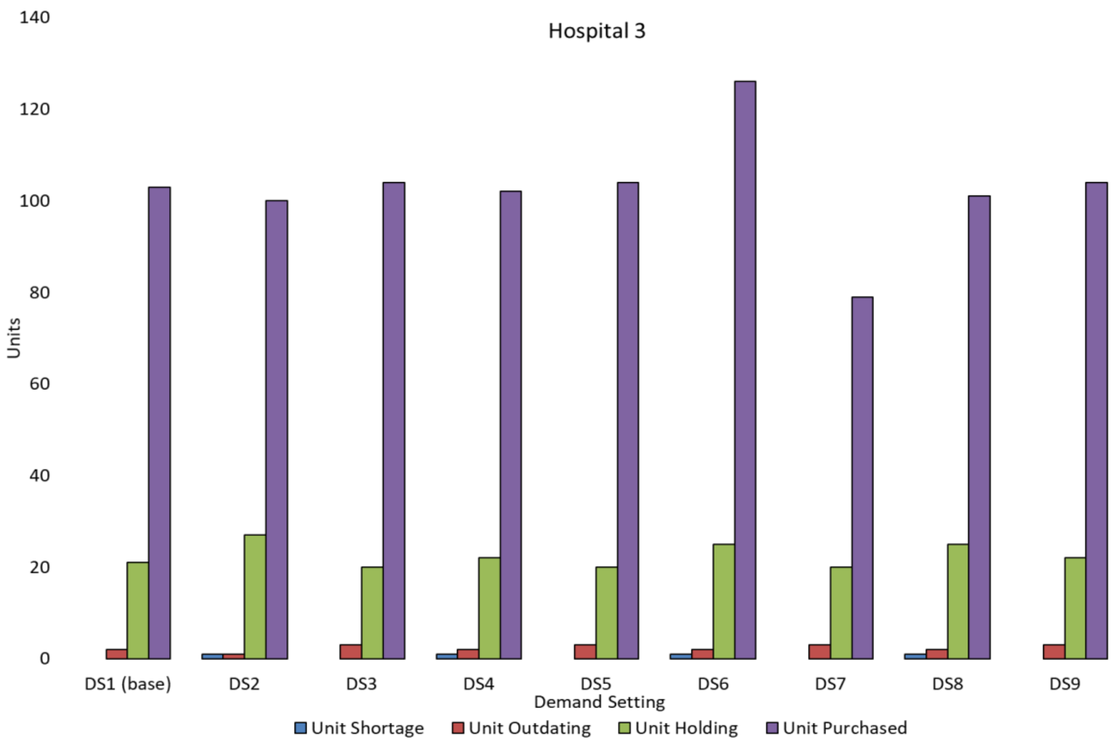


Figure 5.2(c)

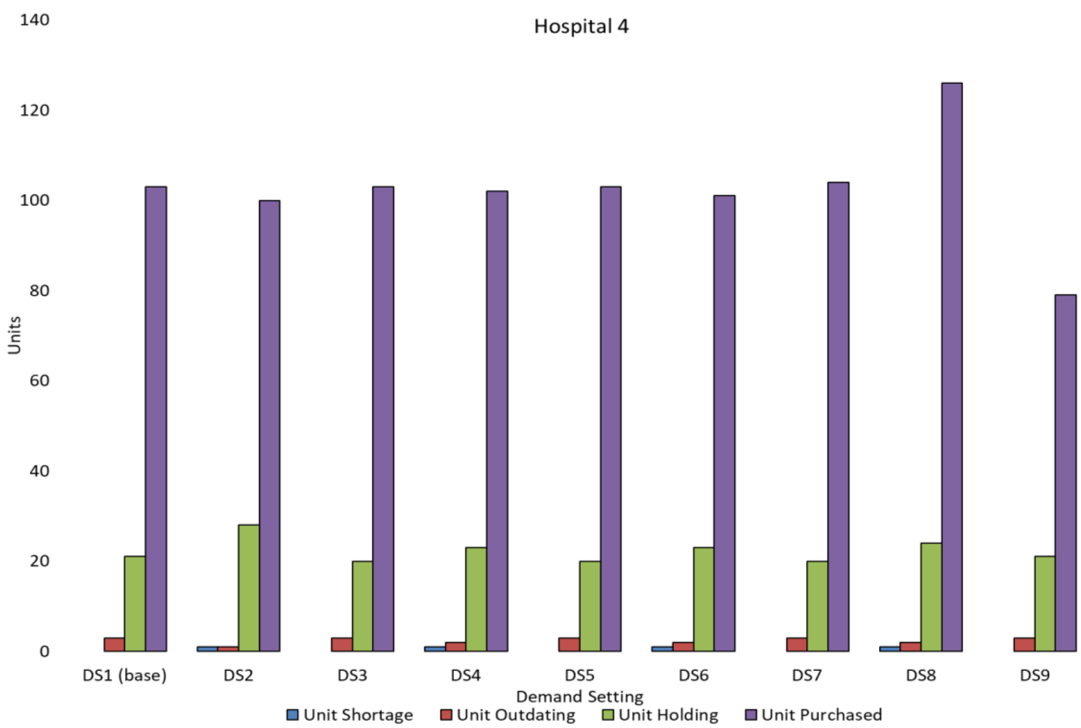


Figure 5.2(d)

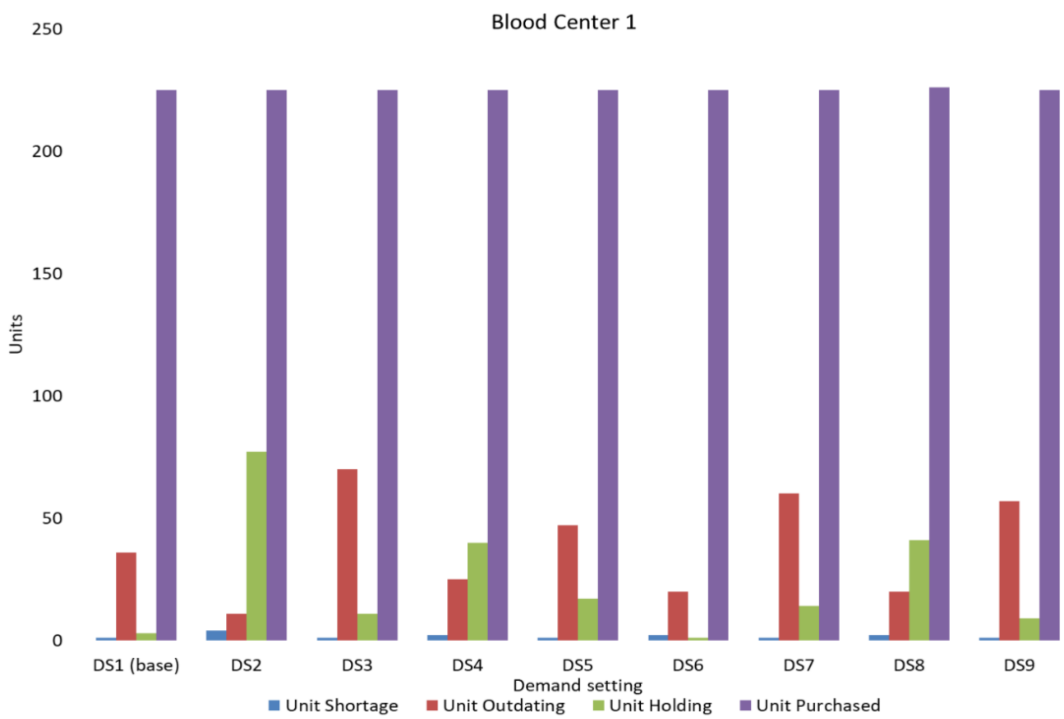


Figure 5.2(e)

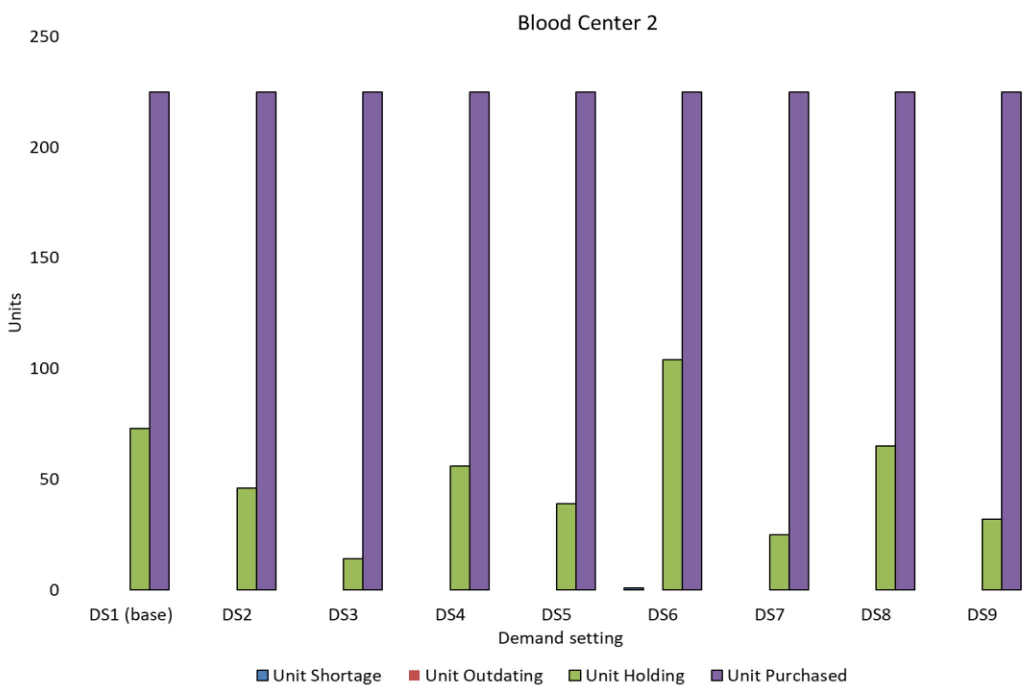


Figure 5.2(f)

Figure 5.2(a)-(f): Impact of Various Demand Settings on Performance Measures of Blood Supply Chain

5.5.2 Variation in the Mean Supply

While Section 5.5.1 discusses the effect of mean demand on the performance measures, the mean platelet supply is altered in this section (Table 5.5). SS1 represents the base case, whereas the mean supply for blood center #1 is altered in supply settings 2 (SS2) and 3 (SS3) by a factor of 1.25 and 0.75, respectively. This procedure is similarly repeated for blood center 2 under supply settings 4 and 5 (SS4 and SS5).

At the hospital level, it is observed that the units outdated, holding and purchased increase for settings SS2 and SS4 and decrease for SS3 and SS5 when compared to the base case (SS1). This is primarily because of the rise in the total supply of blood units in the former settings at the BCs, and hence, more units are purchased by hospitals (to avoid shortage), leading to more units held in inventory and more outdating. The performance measures for hospitals #3 and #4 are extremely similar to each other for all conditions, while hospital #1 has the highest values for all the critical attributes. Figure 5.3(a) – (f) exhibits the performance measures of the supply chain in the present study.

As one would foresee, an increase in supply at blood center #1 results in a surge in the outdated units, whereas the opposite pattern is observed for SS2. As anticipated, SS2 and SS3 have an insignificant impact on the performance measures for blood center #2. The comprehensive cost measures for different supply scenarios are presented in Table 5.6. It can be noted that the average cost per day per scenario is the least for SS1 compared to the other supply settings.

Table 5.5: Various Supply Settings Considered in the Present Study

Setting	Hospital 1		Hospital 2		Hospital 3		Hospital 4		Blood Center 1		Blood Center 2	
	Mean	STD	Mean	STD	Mean	STD	Mean	STD	Mean	STD	Mean	STD
SS1 (base)	150	24	50	8	100	16	100	16	225	37	225	37
SS2	150	24	50	8	100	16	100	16	**281**	**37**	225	37
SS3	150	24	50	8	100	16	100	16	**169**	**37**	225	37
SS4	150	24	50	8	100	16	100	16	225	37	**281**	**37**
SS5	150	24	50	8	100	16	100	16	225	37	**169**	**37**

Table 5.6: Overall Cost Measure for Various Supply Settings

Setting	Average cost per day per scenario (Best, Worst, STD)
SS1 (base)	3,253 (3,168, 3375, 40)
SS2	3,455 (3,358, 3559, 41)
SS3	3,456 (3,198, 3940, 135)
SS4	3,446 (3,347, 3523, 35)
SS5	3,449 (3,180, 3767, 138)

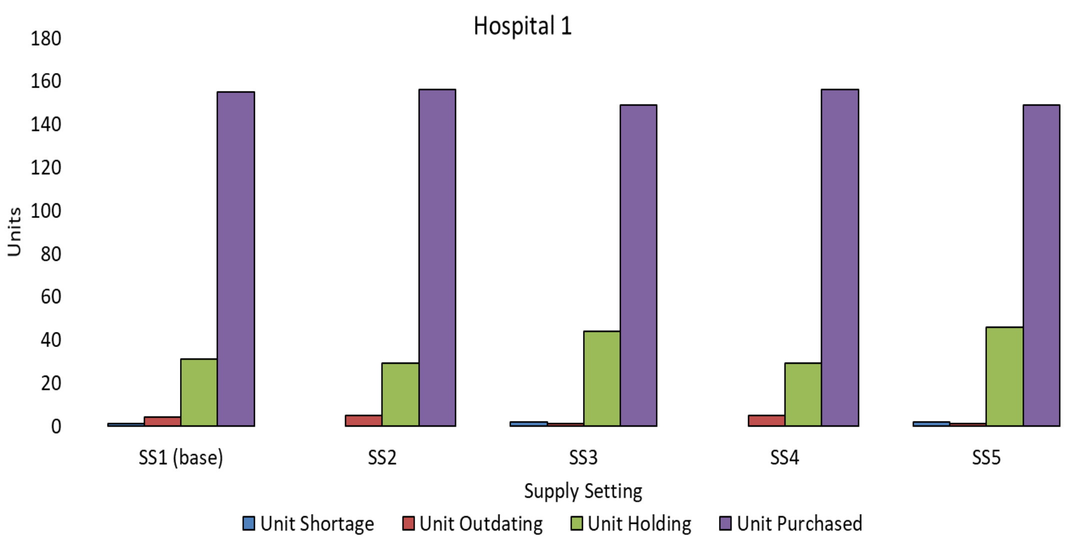


Figure 5.3(a)

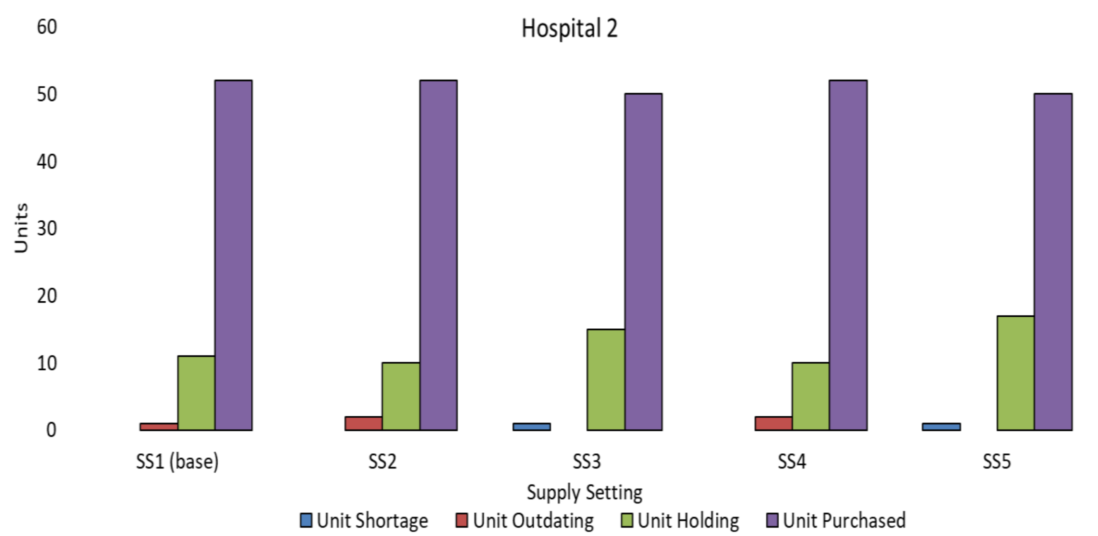


Figure 5.3(b)

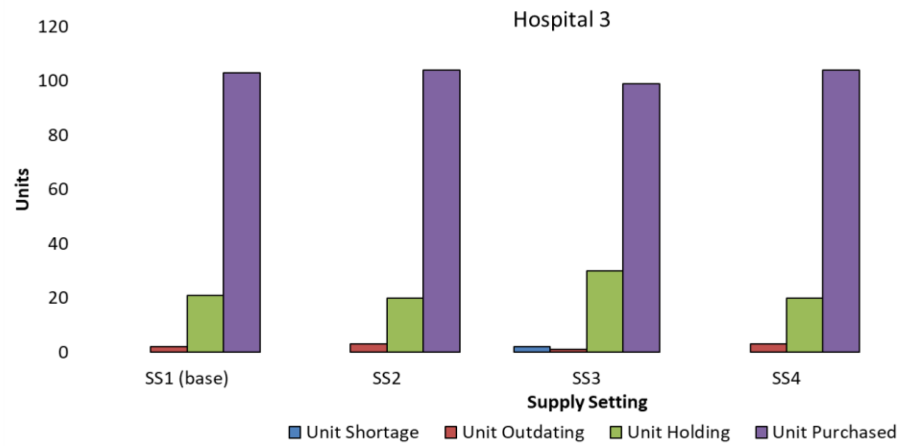


Figure 5.3(c)

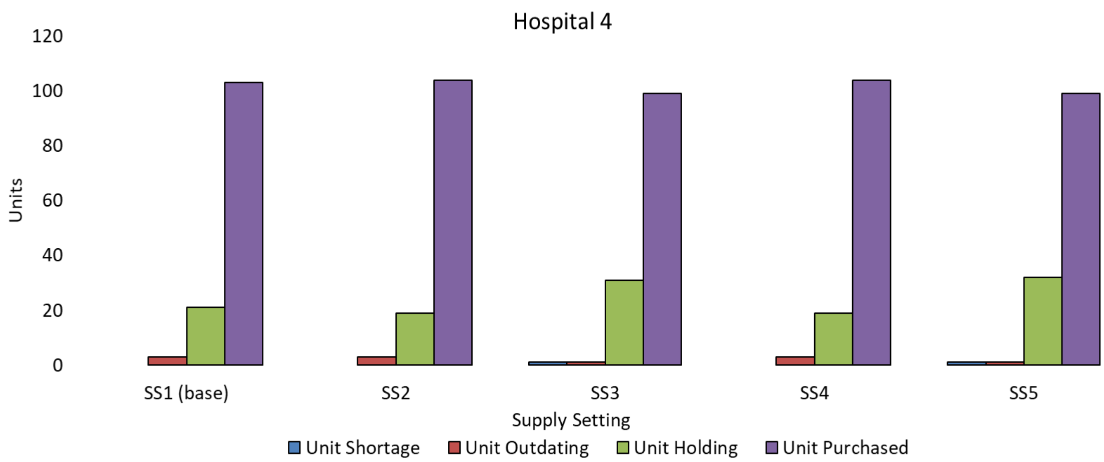


Figure 5.3(d)

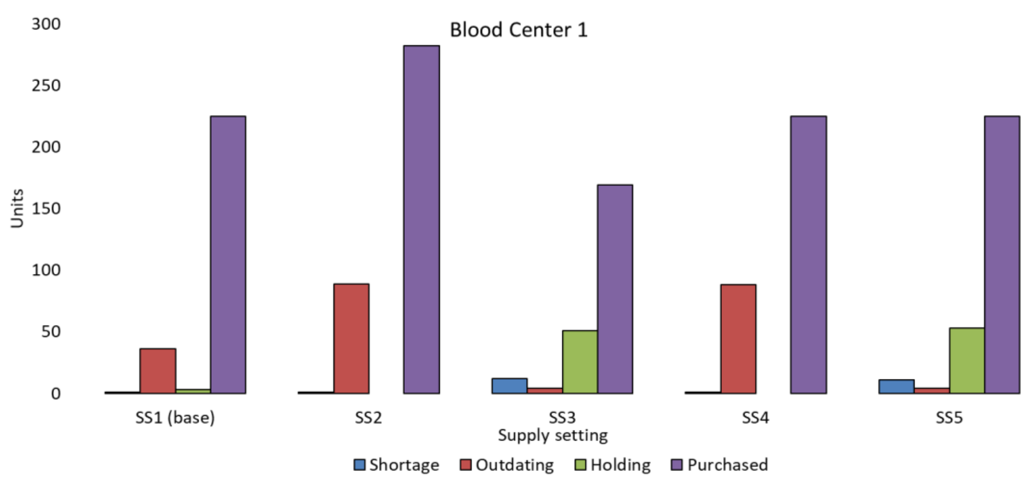


Figure 5.3(e)

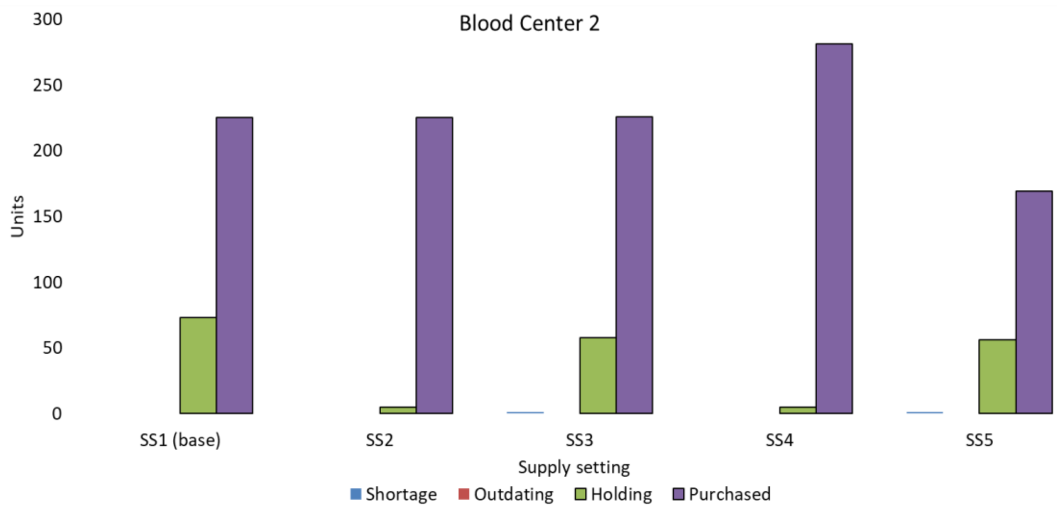


Figure 5.3(f)

Figure 5.3(a)-(f): Impact of Various Supply Settings on Performance Measures of Blood Supply Chain

5.5.3 Impact of Changes in Coefficient of Demand Variation

The changes in the coefficient of variation (CV) in steps of 0.1 for demand at the hospitals are shown in Table 5.7. CV is the ratio of standard deviation with the mean of the blood platelet demand. The units purchased by the hospitals are relatively constant to their mean values as CV increases. However, with the linear rise in CV, the average units outdated, shortage, inventory increases almost linearly. This is because the increase in CV leads to an increase in the variation of platelet demand. Due to an increase in the variation, high demand fluctuation is experienced, resulting in more units are held in inventory, leading to an increase in units expired. Figure 5.4(a) – (f) shows the impact of the demand variation on the hospitals and the blood centers. Since the units ordered by hospitals to the blood center is almost constant, the performance measures of the blood center are insignificantly impacted by the change in the CV. Also, from Figure 5.5, it is evident that the total cost increases with the inflation in the CV. This is expected due to the increase in unit shortage, outdating, and inventory with the upward trend in the CV.

Table 5.7: Coefficient of Variation (CV) for Demand Settings

Setting	Hospital #1	Hospital #2	Hospital #3	Hospital #4	Blood Center #1	Blood Center #2
CVDS1 (CV = 0.1)	N ~ (150, 15)	N ~ (50, 5)	N ~ (100, 10)	N ~ (100, 10)	N~ (225, 37)	N~ (225, 37)
CVDS2 (CV = 0.2)	N ~ (150, 30)	N ~ (50, 10)	N ~ (100, 20)	N ~ (100, 20)	N~ (225, 37)	N~ (225, 37)
CVDS3 (CV = 0.3)	N ~ (150, 45)	N ~ (50, 15)	N ~ (100, 30)	N ~ (100, 30)	N~ (225, 37)	N~ (225, 37)
CVDS4 (CV = 0.4)	N ~ (150, 60)	N ~ (50, 20)	N ~ (100, 40)	N ~ (100, 40)	N~ (225, 37)	N~ (225, 37)
CVDS5 (CV = 0.5)	N ~ (150, 75)	N ~ (50, 25)	N ~ (100, 50)	N ~ (100, 50)	N~ (225, 37)	N~ (225, 37)

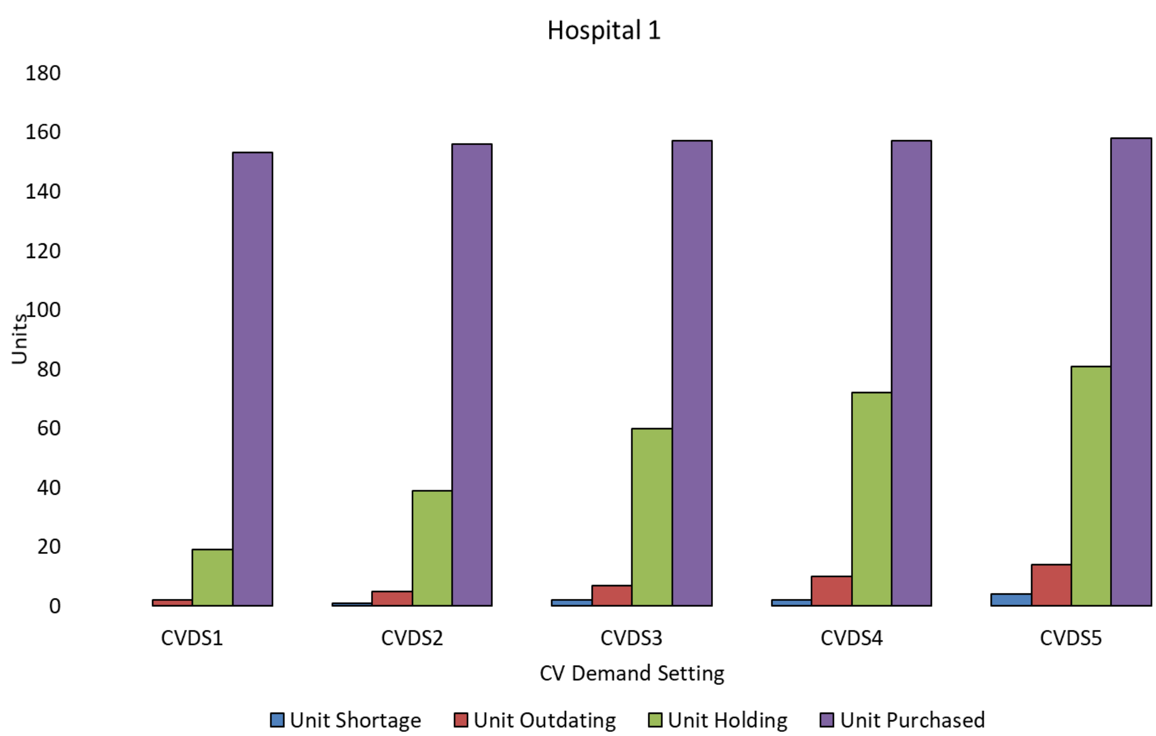


Figure 5.4(a)

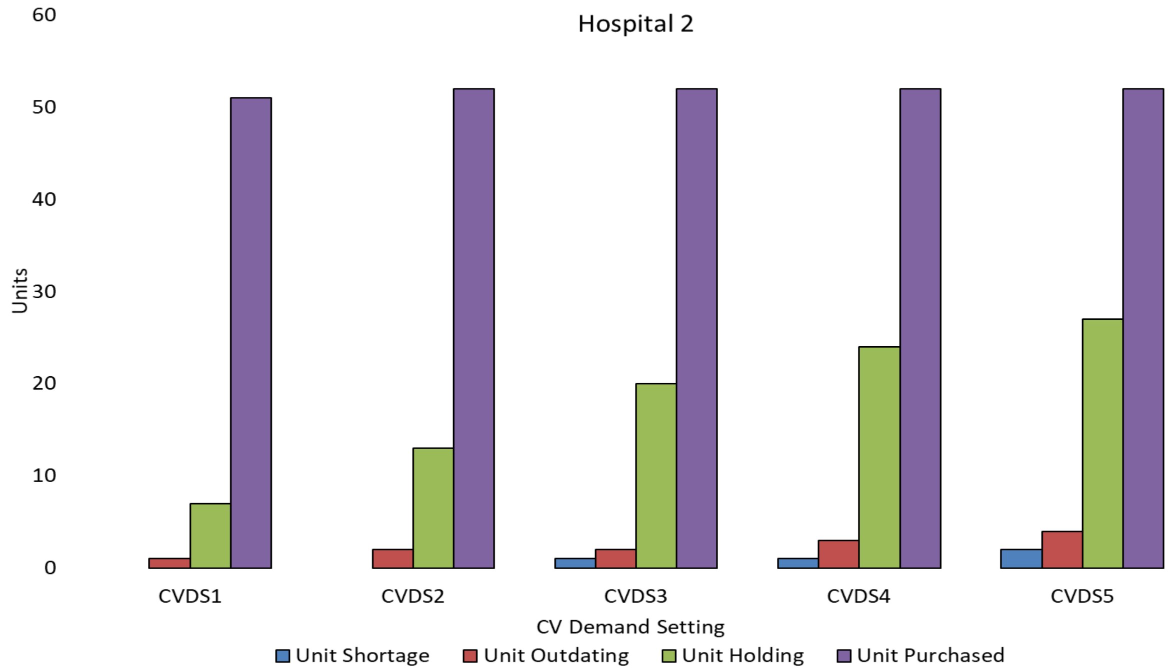


Figure 5.4(b)

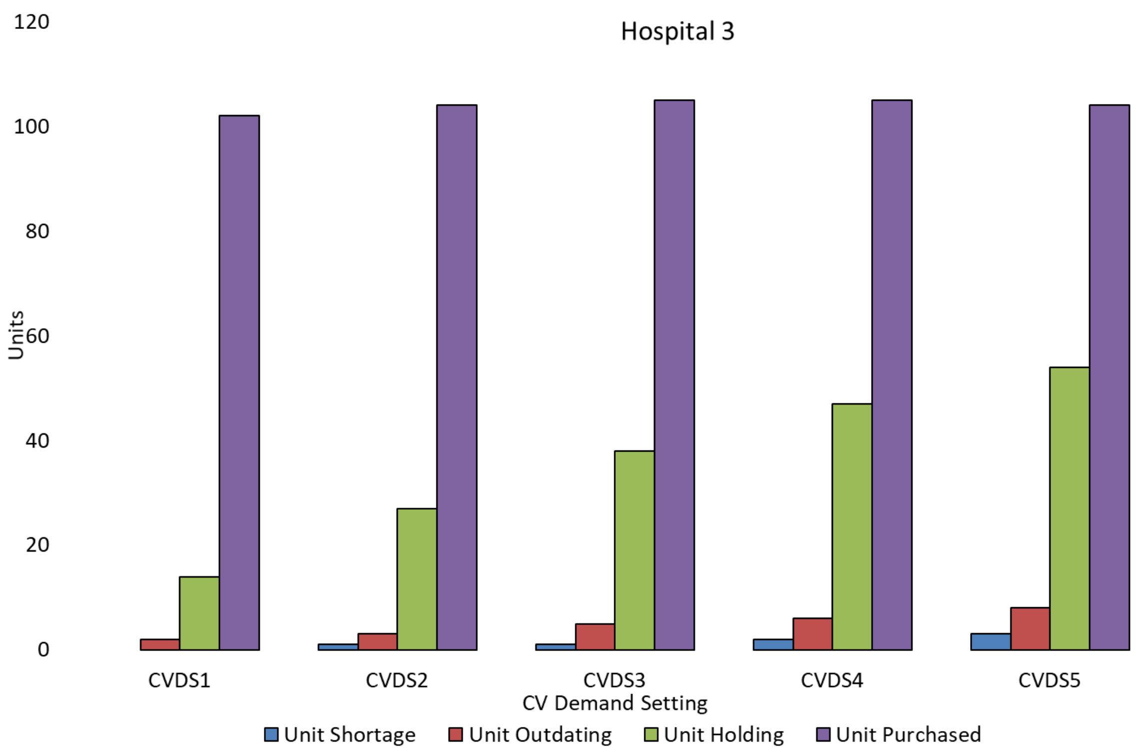


Figure 5.4(c)

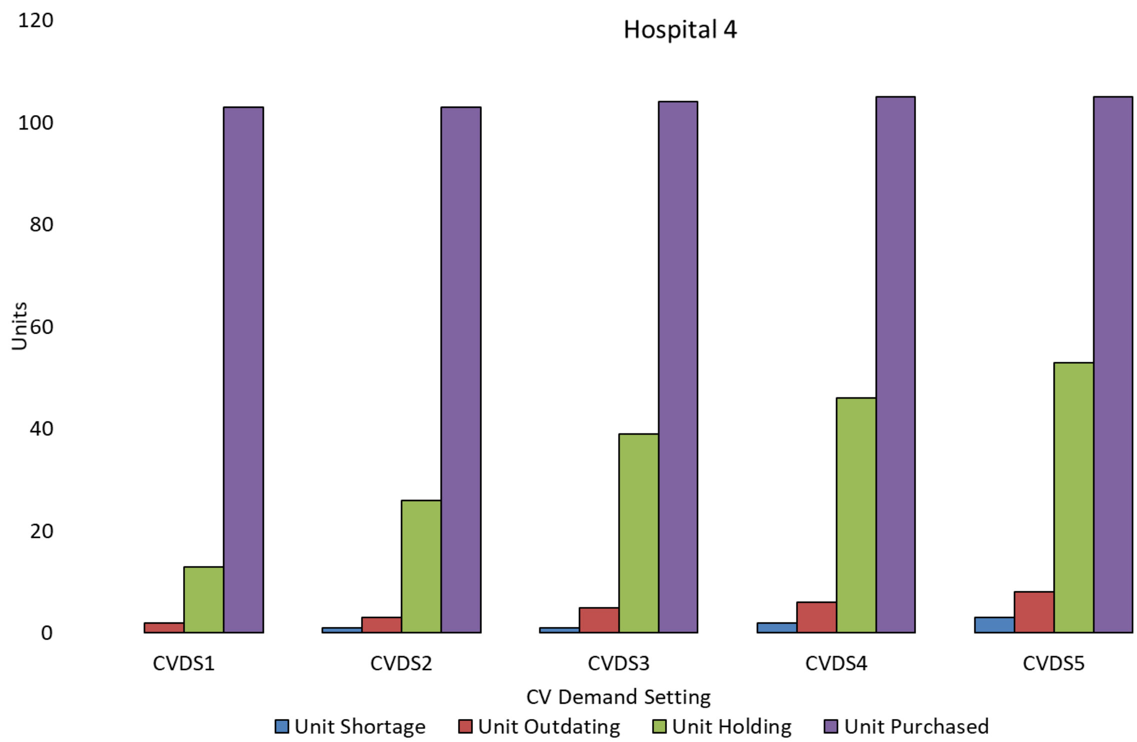


Figure 5.4(d)

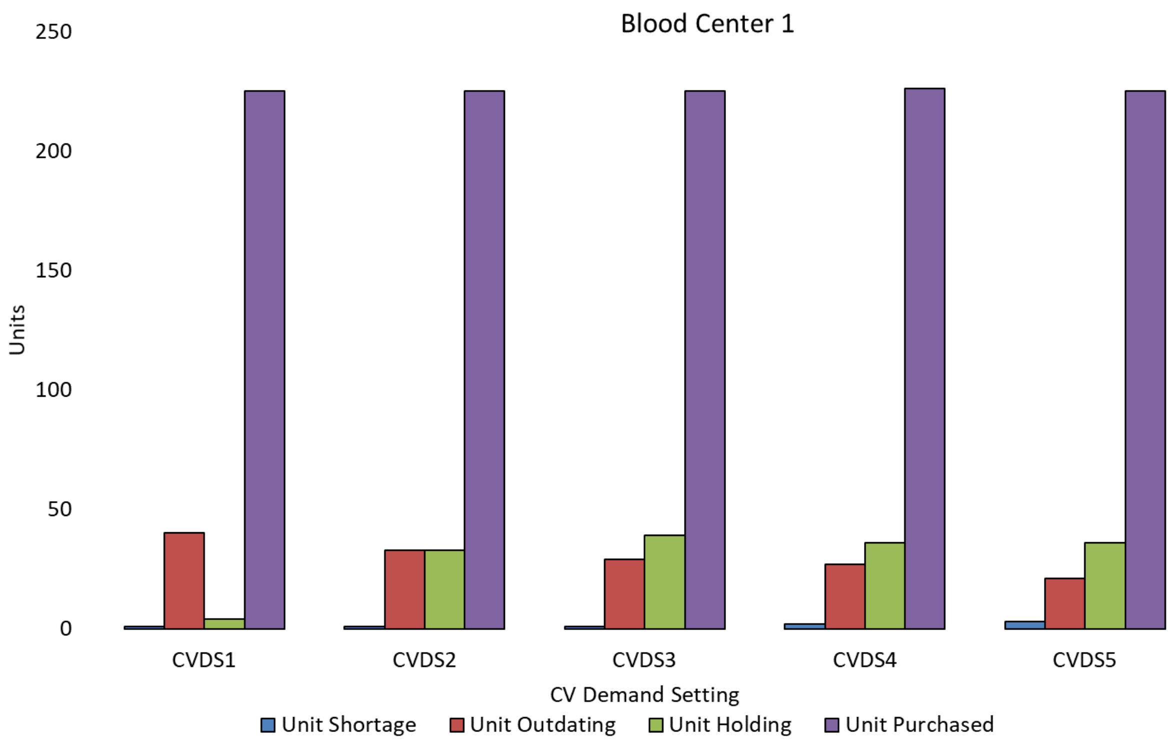


Figure 5.4(e)

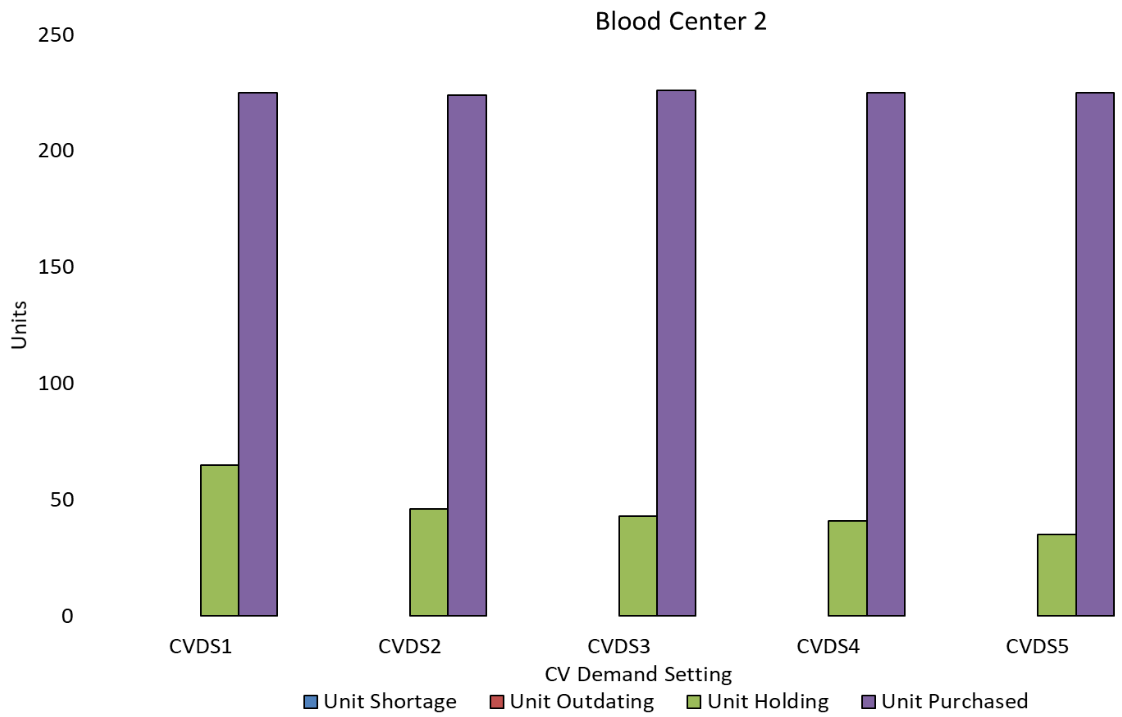


Figure 5.4(f)

Figure 5.4(a)-(f): Impact of Changes in Coefficient of Demand Variation at Hospitals and Blood Centers

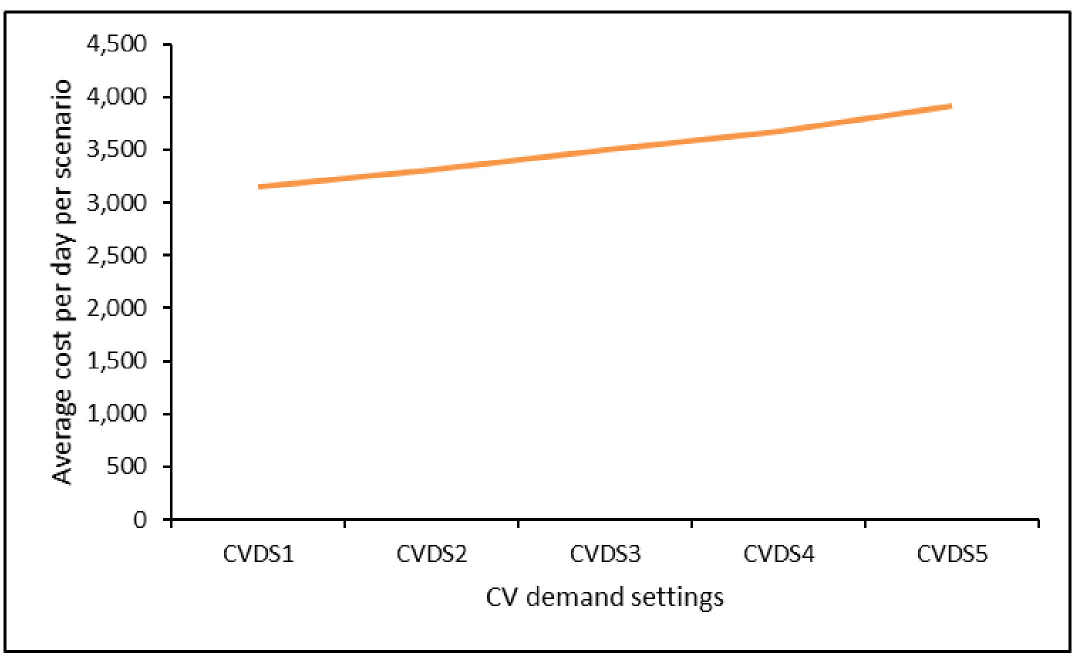


Figure 5.5: Impact of Coefficient of Demand Variation on Total Cost

5.5.4 Impact of Changes in Coefficient of Supply Variation

Table 5.8 depicts the various cases used to analyze the impact of changes in supply settings at the two blood centers in steps of 0.1. It is observed from Figure 5.6(a) – (f) that the units purchased, holding, outdated, and shortage at hospitals are not influenced by the variation in supply. As in the CVDS setting, the units ordered are almost constant. However, with the increase in the supply CV, the units outdated, shortage, and held in inventory increases almost linearly. As in the demand variation setting, from Figure 5.7, it is evident that the total cost increases with the inflation in the supply variation.

Table 5.8: Coefficient of Variation (CV) for Supply Settings

Setting	Hospital #1	Hospital #2	Hospital #3	Hospital #4	Blood Center #1	Blood Center #2
CVSS1 (CV = 0.1)	N ~ (150, 24)	N ~ (50, 8)	N ~ (100, 16)	N ~ (100, 16)	N~ (225, 23)	N~ (225, 23)
CVSS2 (CV = 0.2)	N ~ (150, 24)	N ~ (50, 8)	N ~ (100, 16)	N ~ (100,16)	N~ (225, 45)	N~ (225, 45)
CVSS3 (CV = 0.3)	N ~ (150, 24)	N ~ (50, 8)	N ~ (100, 16)	N ~ (100, 16)	N~ (225, 68)	N~ (225, 68)
CVSS4 (CV = 0.4)	N ~ (150, 24)	N ~ (50, 8)	N ~ (100, 16)	N ~ (100, 16)	N~ (225, 90)	N~ (225, 90)
CVSS5 (CV = 0.5)	N ~ (150, 24)	N ~ (50, 8)	N ~ (100, 16)	N ~ (100, 16)	N~ (225, 113)	N~ (225, 113)

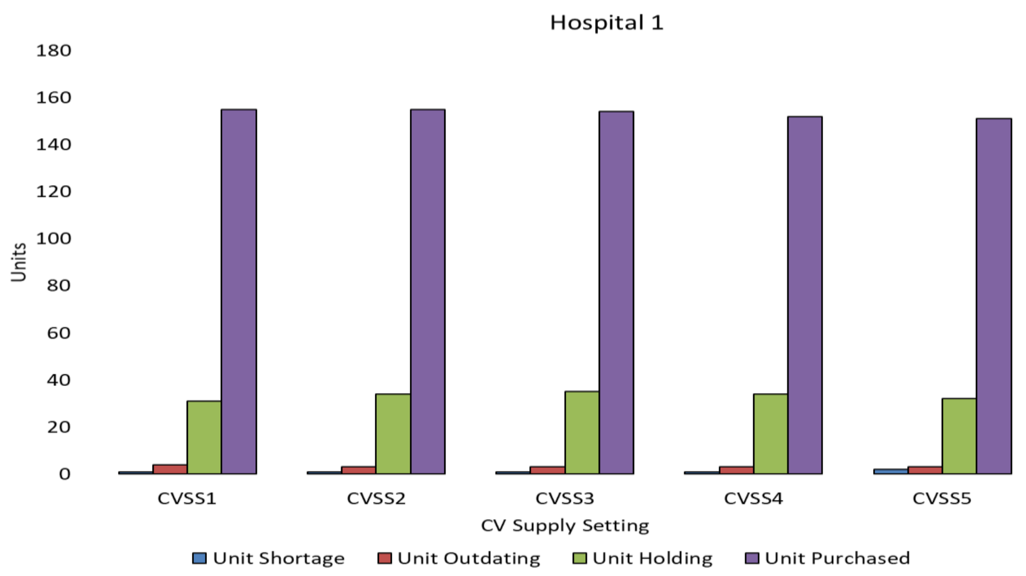


Figure 5.6(a)

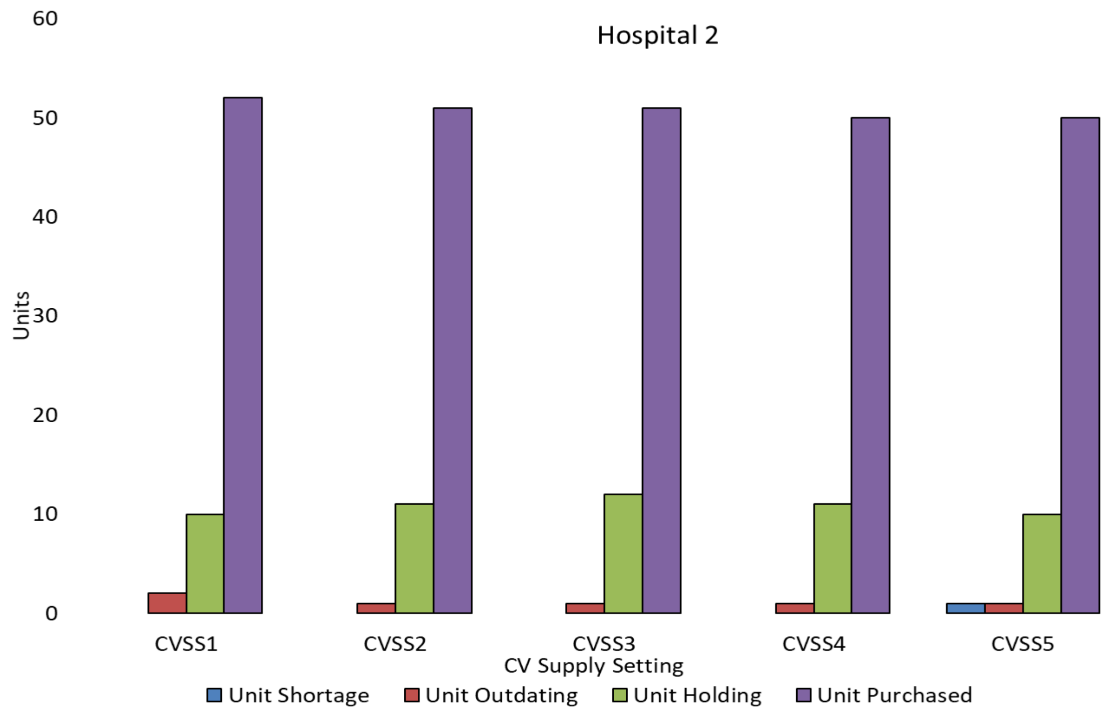


Figure 5.6(b)

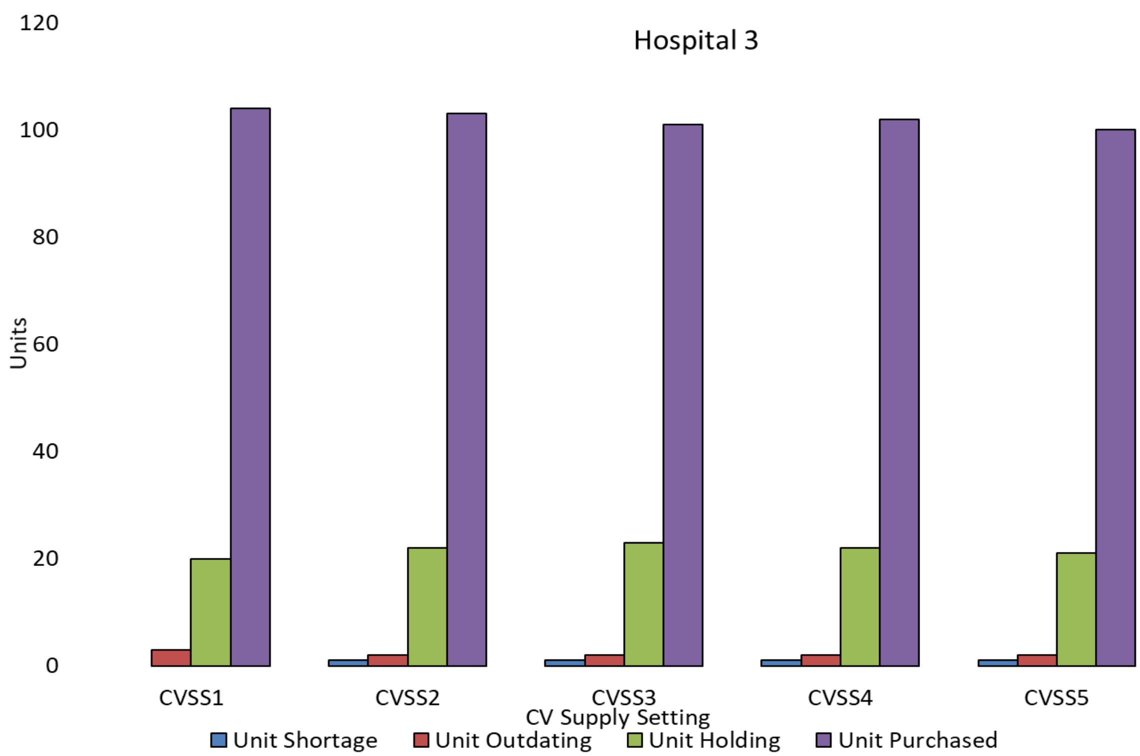


Figure 5.6(c)

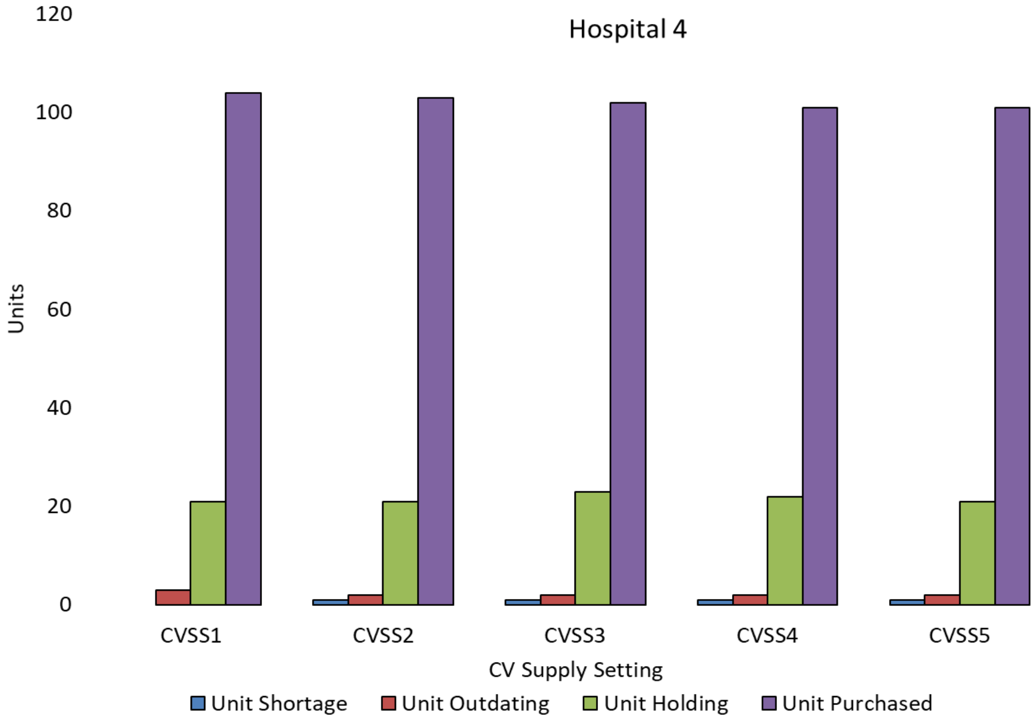


Figure 5.6(d)

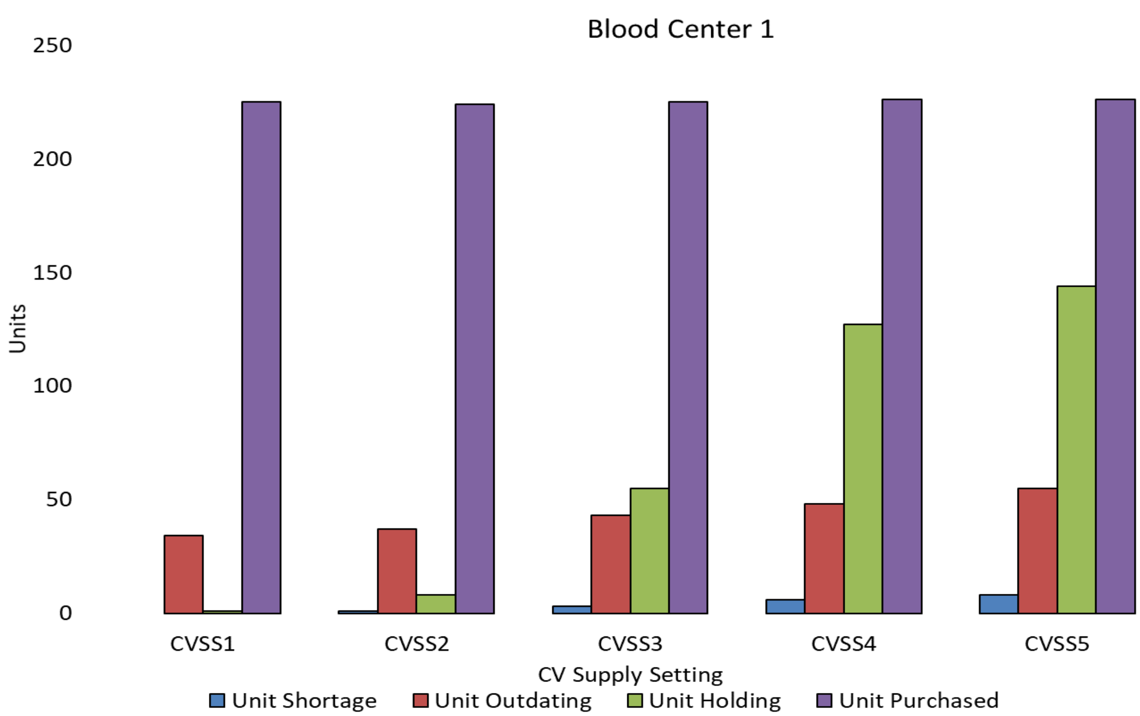


Figure 5.6(e)

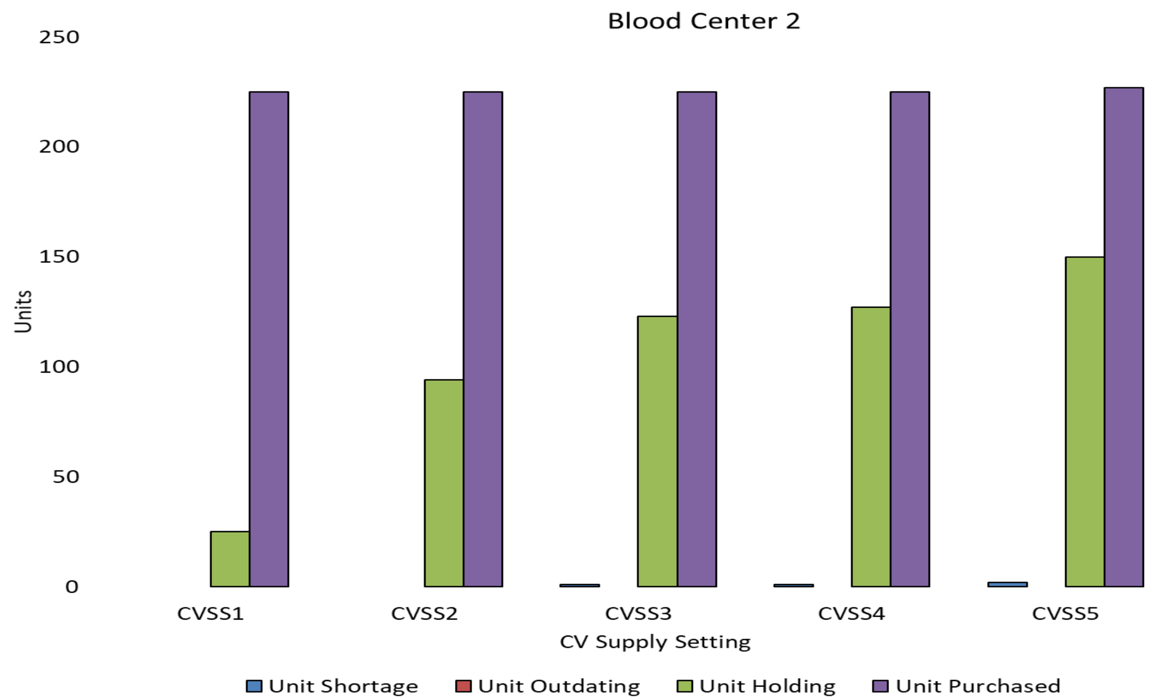


Figure 5.6(f)

Figure 5.6(a)-(f): Impact of Coefficient of Supply Variation on Performance Measures at Hospitals and Blood Centers

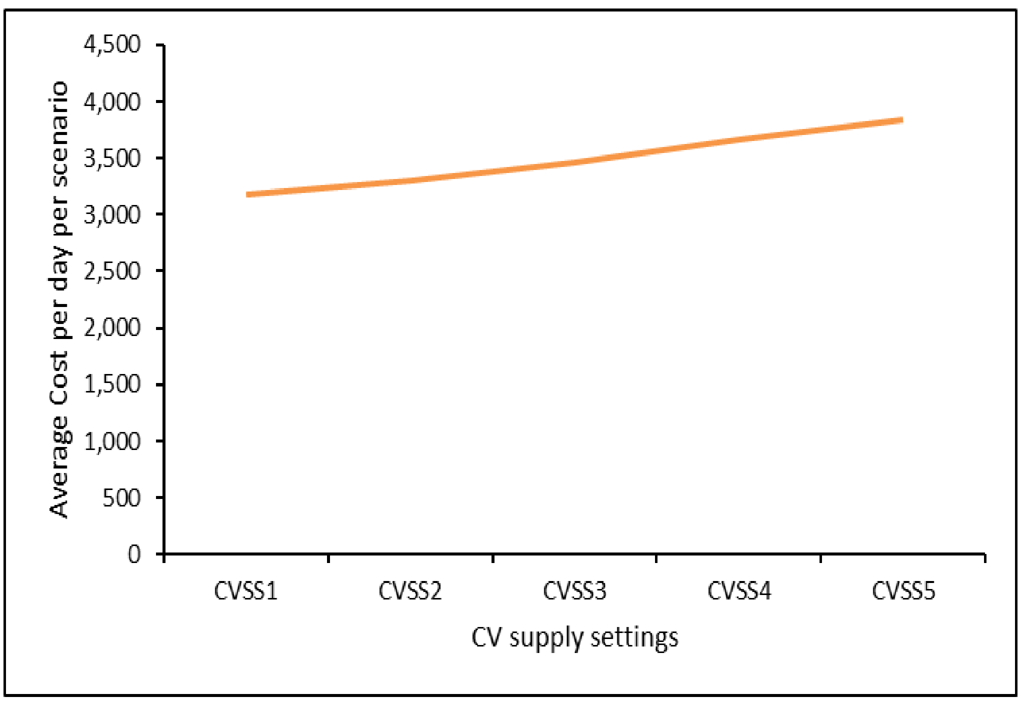


Figure 5.7: Impact of Coefficient of supply variation on total cost

5.5.5 Impact of Changes in the Cost Settings

Table 5.9 summarizes the various cost settings used in this study (derived from Rajendran and Ravindran, 2019). The base case is represented by CS1, while CS2 - CS10 are generated from multiplying one cost element (i.e., Inventory Holding Cost (IHC), Shortage Cost (SC), Outdating Cost (OC), Fixed Transportation Cost (FTC) and Variable Purchasing Cost (VPC)) with 0.5, whereas CS11 - CS19 is obtained from multiplying each cost component with 1.5 while maintaining the other costs at their base level. Figure 5.8(a) – (f) showcases the impact of these cost setting changes for all medical facilities and blood centers, respectively. The inventory units are observed to be fluctuating for both the blood centers. While blood center #2 has a greater number of units holding when compared to blood center #1, only four cost settings display stocks exceeding the base case. This is primarily because of a significantly lower amount of units in inventory at blood center #1. Also, as expected, it has higher values of outdated units aligning with the results found in the previous sections. The impact of variation in CS on the total cost of the supply chain is demonstrated in Table 5.10. As expected, CS2 - CS10 exhibits a lower cost than base case, whereas CS11 - CS19 shows an increased cost in the supply chain.

Table 5.9: Cost Settings

Cost setting	Cost incurred at blood centers			Cost incurred at hospitals					
	IHC	**SC**	**OC**	**FTC(H1,H2,H3, H4) from BC1**	**FTC(H1,H2,H3, H4) from BC2**	**IHC**	**VPC**	**SC**	**OC**
CS1(base)	108	2,690	538	113,225,339,675	339,675,113,225	130	650	3,250	650
CS2	**54**	2,690	538	113,225,339,675	339,675,113,225	130	650	3,250	650
CS3	108	**1,345**	538	113,225,339,675	339,675,113,225	130	650	3,250	650
CS4	108	2,690	**269**	113,225,339,675	339,675,113,225	130	650	3,250	650
CS5	108	2,690	538	**56,112,169,337**	339,675,113,225	130	650	3,250	650
CS6	108	2,690	538	113,225,339,675	**169,337,56,112**	130	650	3,250	650
CS7	108	2,690	538	113,225,339,675	339,675,113,225	**65**	650	3,250	650
CS8	108	2,690	538	113,225,339,675	339,675,113,225	130	**325**	3,250	650
CS9	108	2,690	538	113,225,339,675	339,675,113,225	130	650	**1,625**	650
CS10	108	2,690	538	113,225,339,675	339,675,113,225	130	650	3,250	**325**
CS11	**162**	2,690	538	113,225,339,675	339,675,113,225	130	650	3,250	650
CS12	108	**4,035**	538	113,225,339,675	339,675,113,225	130	650	3,250	650
CS13	108	2,690	**807**	113,225,339,675	339,675,113,225	130	650	3,250	650
CS14	108	2,690	538	**169, 337, 508, 1,012**	339,675,113,225	130	650	3,250	650
CS15	108	2,690	538	113,225,339,675	**508, 1,012, 169, 337**	130	650	3,250	650
CS16	108	2,690	538	113,225,339,675	339,675,113,225	**195**	650	3,250	650
CS17	108	2,690	538	113,225,339,675	339,675,113,225	130	**975**	3,250	650
CS18	108	2,690	538	113,225,339,675	339,675,113,225	130	650	**4,875**	650
CS19	108	2,690	538	113,225,339,675	339,675,113,225	130	650	3,250	**975**

Table 5.10: Impact of CS on Total Cost of Supply Chain

Setting	Average Cost/Per day/per scenario (Best, Worst, STD)
CS1(base)	3,253 (3,168, 3,375, 40)
CS2	3,191 (3,115, 3,324, 41)
CS3	3,225 (3,130, 3,314, 38)
CS4	3,128 (3,046, 3,262, 43)
CS5	3,247 (3,145, 3,356, 42)
CS6	3,249 (3,167, 3,375, 39)
CS7	3,189 (3,119, 3,320, 41)
CS8	3,191 (3,092, 3,264, 33)
CS9	3,183 (3,114, 3,270, 36)
CS10	3,218 (3,137, 3,308, 34)
CS11	3,283 (3,168, 3,433, 48)
CS12	3,263 (3,168, 3,389, 46)
CS13	3,334 (3,225, 3,462, 48)
CS14	3,254 (3,143, 3,350, 47)
CS15	3,253 (3,171, 3,378, 39)
CS16	3,296 (3,207, 3,396, 40)
CS17	4,595 (4,488, 4,719, 45)
CS18	3,269 (3,172, 3,371, 42)
CS19	3,283 (3,186, 3,394, 42)

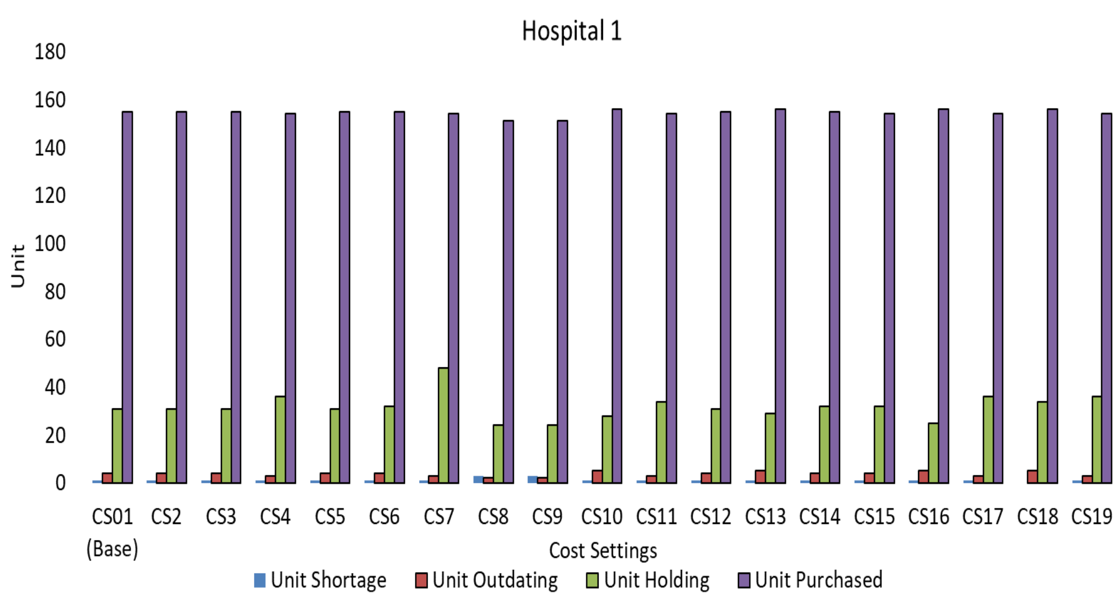


Figure 5.8(a)

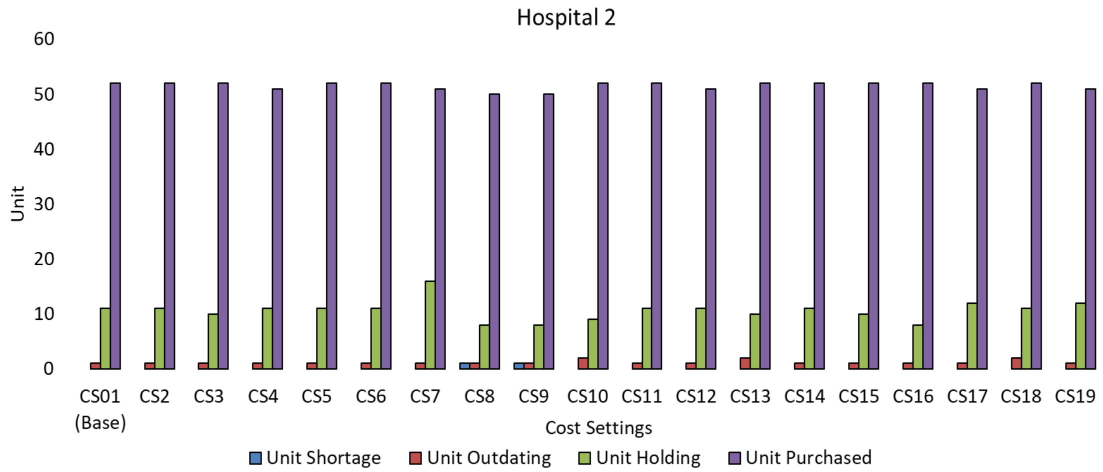


Figure 5.8(b)

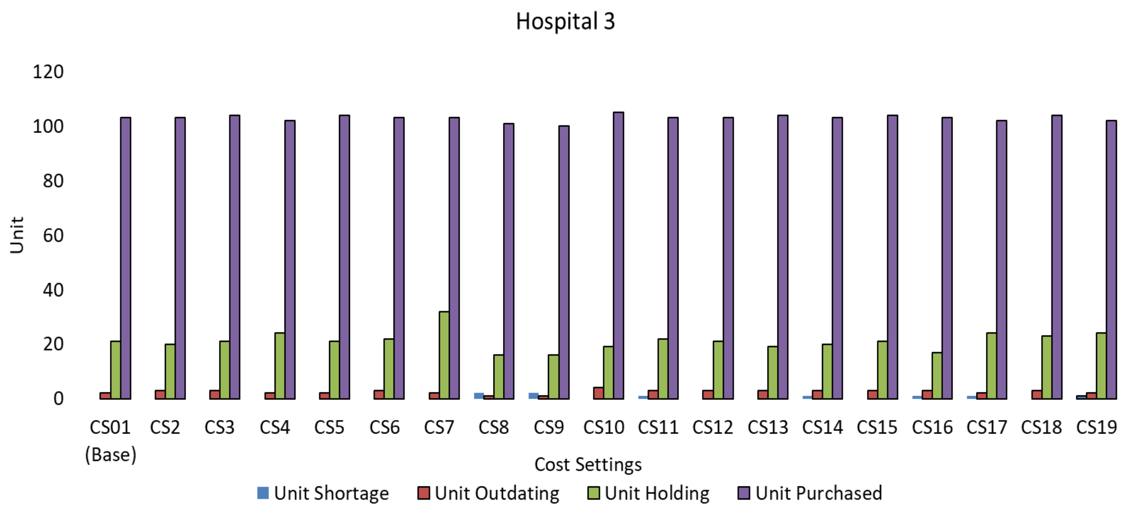


Figure 5.8(c)

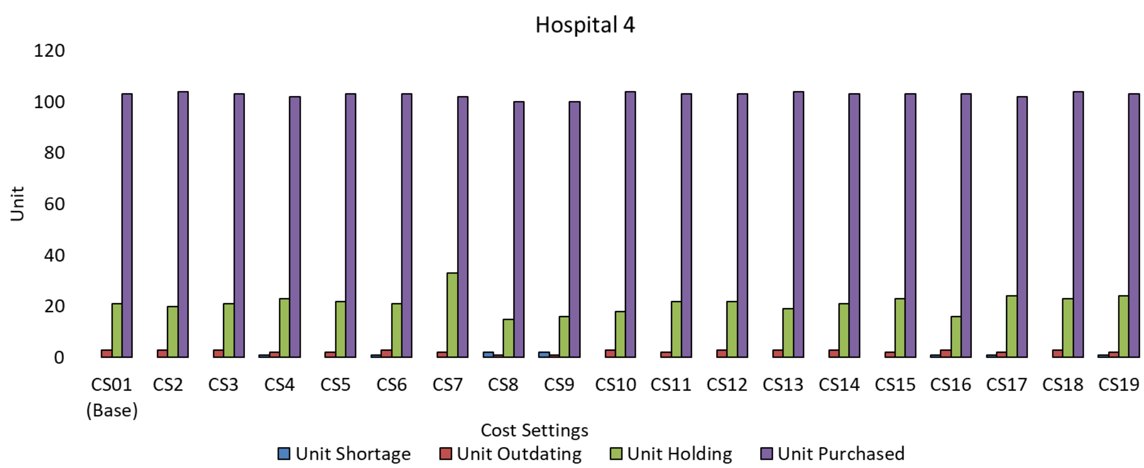


Figure 5.8(d)

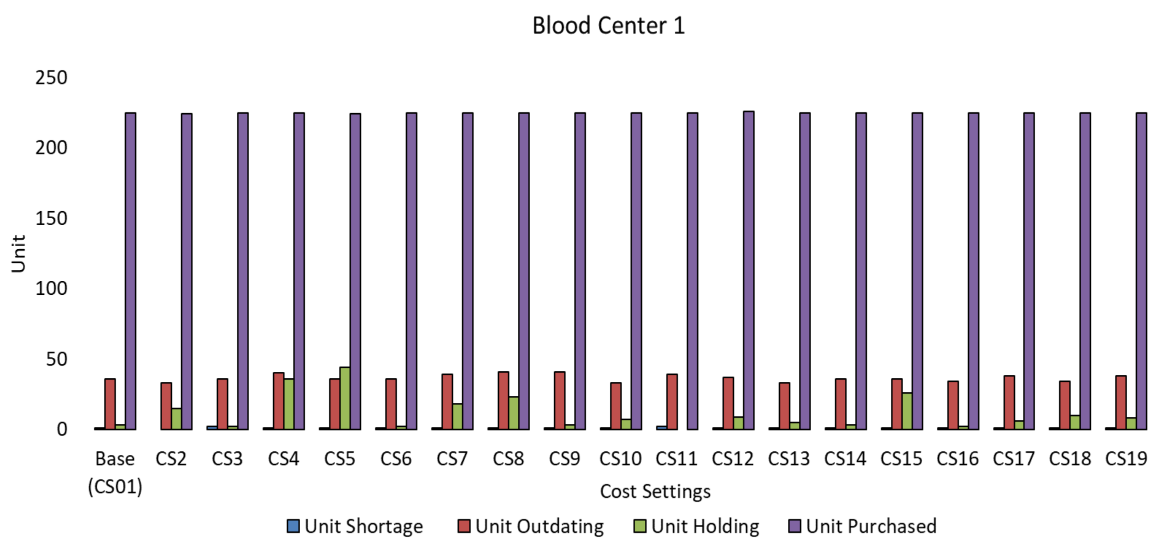


Figure 5.8(e)

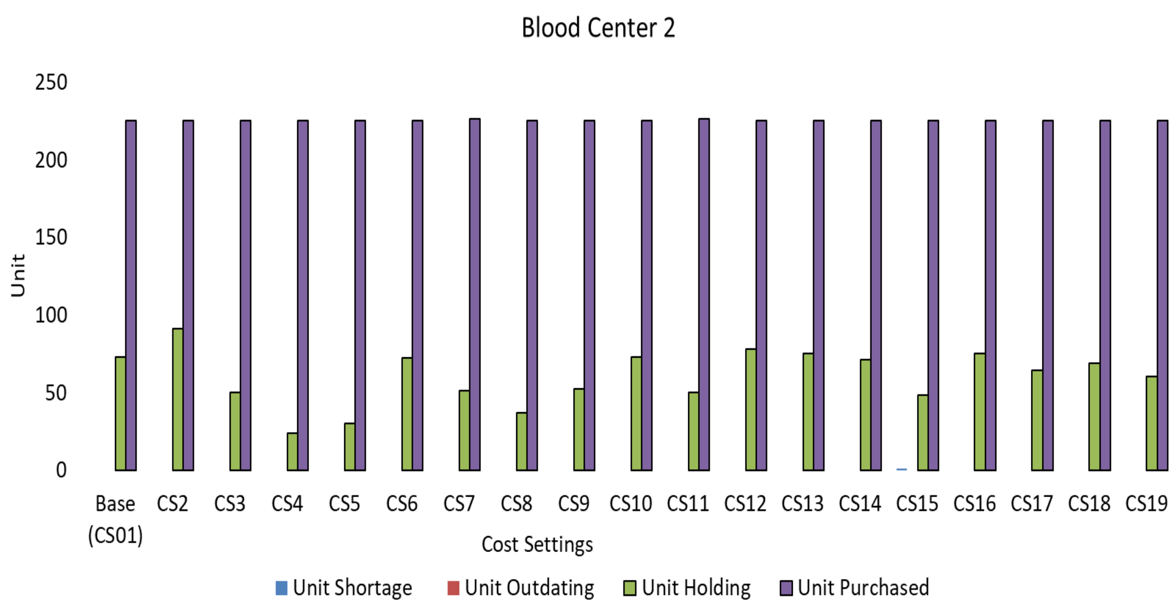


Figure 5.8(f)

Figure 5.8(a)-(f): Impact of CS on Hospitals and Blood Centers

5.6 Implication of Results

The present study investigates the impact of four hospitals and two blood centers solved using Python with Gurobi optimizer. The model examined the results for nine different demand settings and five distinct supply settings. It is observed that four demand settings (DS 3, 5, 7, and

9) displayed a lower average cost per day per scenario when compared to the base case. At the blood center level, a rise in cost was seen for variation in supply settings causing fluctuations in the units outdating. Sensitivity analysis is conducted by varying cost, supply, and demand variation. The results of sensitivity analysis indicate a significant deviation for the inventory level at the hospitals and blood centers, which leads to a higher average cost in the supply chain. An insignificant change is evident in the shortage and outdating cost for different cost variation settings. In more details, the results indicate that a change in the mean demand has a linear impact on the supply chain cost, whereas the mean supply has a minimal impact on the total cost parameter. Furthermore, an increase in the coefficient of demand variation induces a rise in the total supply chain by 5.55%, while a 4.8% increase is observed when varying the coefficient of supply variation parameter

Based on the computational results, the model is robust for all settings and can easily be extended to include more sites in the supply chain. Procuring emergency units from other blood centers to compensate for shortages and reduce unit outdating would improve the functionality of the system and prevent hundreds of surgeries from being canceled each day. The developed framework in the present study can be easily extended for other similar supply chains having unpredictable supply and demand and deals with perishable products. In chapter 6, goal programming can be considered to include multiple objective functions, such as minimization of outdating and inventory at blood centers and maximize efficiency. Also, the impact of various ordering policies can be studied on the blood supply chain consisting of *X* blood centers and *K* hospitals. Furthermore, other blood components, such as RBC, WBC, and plasma, could also be included in the supply chain.

CHAPTER 6

MULTIPLE CRITERIA DECISION MAKING FOR THE BLOOD SUPPLY CHAIN

6.1 Multiple Criteria Decision Making

Previous chapters have focused on developing mathematical models to investigate blood supply inventory management. The objective function comprised of multiple cost components, such as unit purchasing, transportation, inventory, and outdated. However, in reality, some cost elements such as shortage and outdating cannot be accurately measured in the same units. Therefore, the present study proposes a mathematical model based on multi-criteria decision-making (MCDM) techniques considering different conflicting objective functions for a BSC comprising of k hospitals and one blood center. The model from Chapter 4 is incorporated with multiple criteria to formulate the multiple objective models and implemented in Section 6.4.

6.2 Solution Approaches

There are several methods for solving multi-objective optimization problems, such as Goal Programming, Compromise Programming, and weighted objective method (Masud & Ravindran, 2008). The Goal programming methods and weighted objective methods are commonly used in practice and will be chosen in this study.

6.2.1 Goal Programming Methodology

Goal programming (GP) is a broadly used method to resolve multi-objective optimization problems. The basic idea is to specify a set of targets or goals for the objectives and minimize the deviations from the targets. The deviations from each target should be minimized, with the assigned priority or weight according to each objective's relative importance. There are several types of goal programming models, such as Pre-emptive Goal Programming and Non-preemptive Goal Programming, Tchebycheff (Min-Max) Goal Programming, Fuzzy Goal Programming, etc. (Masud and Ravindran, 2008, 2009; Jones and Tamiz, 2010). The Pre-emptive Goal Programming and Non-preemptive Goal Programming are more commonly used in practice and will be utilized in this chapter. To solve the MCMP problems, the formulation of goal programming (GP) models require the decision maker (DM) to specify an acceptable level of achievement (b_i) for each criteria f_i and assign a weight w_i (ordinal or cardinal) to be associated with the deviation between f_i and

b_i. Assume k goals are considered in the MCMP model with $f_1(x)$, $f_2(x)$, $f_3(x)$…… $f_k(x)$ as k objectives.

The formulation of GP model can be described as follows (Ravindran and Warsing, 2013):

Minimize $Z = \sum_{i=1}^{k}(w_i^+ d_i^+ + w_i^- d_i^-)$

Subject to

$f_i(x) + d_i^+ - d_i^- = b_i$ for $i = 1, \ldots, k$

$g_j(x) \leq 0$ for $j = 1, \ldots, m$

$x_j, d_i^+, d_i^- \geq 0$ for all i and j

Where $f_i(x)$ is ith objective function, $i = 1, \ldots, k$

$g_j(x)$ is jth constraint function, $j = 1, \ldots, m$

d_i^+ and d_i^- are defined as the deviation variables (plus and minus) of deviation from the target value for i^{th} goal.

Since "not to exceed the targets" are the goals in the GP model, the deviations d_1^+, d_2^+, d_3^+ …. and d_k^+ need to be minimized. The targets, b_1, b_2, b_3 and b_k may or may not be reachable depending on their values, and they have to be specified as input to the GP model by the decision maker. The model will try to achieve $f_i(x)$ as close as possible to b_i for objective i. If the goal were to satisfy $f_i(x) \leq b_i$ then only d_i^+ is assigned a positive weight in the objective i, while the weight on d_i^- is set to zero. The set of weights (w_i^+ and w_i^-) may take two forms as given below:

1. Preemptive priorities (ordinal)
2. Non-preemptive weights (cardinal)

Consider pre-specified (cardinal) weights, the specific values are assigned to w_i^+ and w_i^- in a relative scale to represent the DM's "trade-off" in a group of goals. Once w_i^+ and w_i^- are specified, the goal program is reduced to a single objective optimization problem. Preemptive goal programming uses ordinal ranking or preemptive priorities to the goals. In this approach, the goals with lower priorities are performed only after achieving the goals with higher priorities. Thus, preemptive goal programming is essentially a sequential single objective optimization process, in which succeeding optimizations are performed on the alternate optimal solutions of the previously optimized goals at a higher priority.

6.2.1.1 Preemptive Goal Programming (PGP)

In the Preemptive Goal Programming, ordinal ranking is used to assign goals to different priority levels from highest to lowest. Borda count ranking method, rating (scoring) method or Analytic Hierarchy Process (AHP) are several ranking methods to prioritize the goals for the respective objectives. The goal assigned with lower priority will not be considered until the goal with a higher priority is satisfied. The model becomes a sequential optimization problem.

- **PGP Model objective**

Minimize $Z = P_1 d_1^+ + P_2 d_2^+ + P_3 d_3^+ + \cdots . + P_k d_k^+$

Where $P_1,\ P_2$, P_3 ……and P_k are the pre-emptive priorities assigned to goal 1, goal 2, goal 3, …. and goal k respectively, and P_p is given priority p with the assumption that P_p is much higher than P_{p+1}.

That is, goals with lower priority can only be considered after goals with higher priority are achieved. Hence, preemptive goal programming is basically a sequence of single objective optimization problems, in which succeeding optimizations are performed on the alternate optimal solutions of the previously optimized goals with higher priority. The PGP model is stated as follows:

Minimize $Z = P_1 d_1^+ + P_2 d_2^+ + P_3 d_3^+ + \cdots . + P_k d_k^+$

With the constraints

ALL functional constraints

ALL goal constraints

ALL nonnegativity constraints

$OF_1 = v_1^*$

$OF_2 = v_2^*$

.

.

.

$OF_{k-1} = v_{k-1}^*$

Where OF_j is the objective function for the j^{th} priority level and v_j^* is the optimal value of the j^{th} objective function $(1 \leq j \leq k-1)$.

Since preemptive goal programming does not specify a weight to an objective, scaling of the objective is not necessary.

6.2.1.2 Non-Preemptive Goal Programming (NPGP)

Under Non-Preemptive Goal Programming, the weights, w_i should be assigned specific values on a relative scale, representing the relative importance of the goal. The specific values of the weights can be obtained from the Decision Maker (DM) using Borda Count Ranking Method, Rating Method, or Analytic Hierarchy Process (AHP) approaches.

- **NPGP Model objective**

Minimize $Z = w_1 d_1^+ + w_2 d_2^+ + w_3 d_3^+ + \cdots . + w_k d_k^+$

Where w_1, w_2 , w_3 ……and w_k are the weights assigned to goal 1, goal 2, goal 3, …. And goal k respectively.

It is noticed that different units and magnitudes are measured in the goals; the scaling of the objective is needed. On the other hand, if the criteria values are not scaled, a goal with a large magnitude would simply dominate the final result, irrespective of the assigned weights. There are several scaling methods, such as simple scaling, ideal value method, simple linearization and L_p Norm (Ravindran and Warsing, 2013). In this chapter, ideal value methods are used for scaling.

Ideal value represents the optimal value for each objective while disregarding all other objectives. Assume the ideal values (scaling factors) are $\gamma_{1,}$ $\gamma_{2,}$ ….. and γ_k be the ideal values of objectives, the scaled NPGP objective function is given as below:

Minimize $Z = \frac{w_1 d_1^+}{\gamma_1} + \frac{w_2 d_2^+}{\gamma_2} + \frac{w_3 d_3^+}{\gamma_3} + \cdots . + \frac{w_k d_k^+}{\gamma_k}$

With the constraints

ALL functional constraints

ALL goal constraints

ALL nonnegativity constraints

Where w_1, w_2 , w_3 ……and w_k are the weights assigned to goal 1, goal 2, goal 3, …. and goal k respectively. $\gamma_{1,}$ $\gamma_{2,}$ ….. and γ_k are the ideal values of objective 1, objective 2, and objective k respectively.

6.2.2 Weight Objective Method (WOM)

The weighted objective method involves assigning weights to different criteria. By doing so, it allows the decision-maker to take into account the difference in importance between criteria. Assigning weights for the objectives is critical, and an appropriate weight allocation should be consistent with the decision maker's preference. The weight assigned to each objective illustrates the relative importance of the objective. The weights and ratings can be obtained by Borta Count or AHP methods. AHP method is one of the most popular methods in estimating decision maker's preference. Since the magnitude can affect the results, appropriate scaling methods need to be used. To apply the weighted objective method, it is essential to scale each objective.

Assume the ideal values (scaling factors) are $\gamma_{1,}\ \ \gamma_{2,}\ \ldots..$ and γ_k be the ideal values of objectives; the scaled WOM objective function is given as below:

Minimize $Z = \frac{w_1 Z_1}{\gamma_1} + \frac{w_2 Z_2}{\gamma_2} + \frac{w_3 Z_3}{\gamma_3} + \cdots . + \frac{w_k Z_k}{\gamma_k}$

With the constraints

ALL functional constraints

ALL nonfunctional constraints

Where $Z_1,\ Z_2$, Z_3 ……and Z_k are the objective for objective 1, objective 2, objective 3, …. and objective k respectively, $w_1,\ w_2$, w_3 ……, and w_k are the weights assigned to goal 1, goal 2, goal 3, …. and goal k respectively, and $\gamma_{1,}\ \ \gamma_{2,}\ \gamma_{3,}$ ….. and γ_k are the ideal values of objective 1, objective 2, objective 3, …. and objective k respectively.

6.3 Identifying the Ideal Values and Target Values

Ideal values for each objective are acquired by optimizing each objective individually while ignoring all other objectives. The target values for each objective are set at 105% of the ideal values for each objective. For example, the ideal (minimum) value for cost objective is $200,000, the target value for the cost is set at $205,000, and the goal is to minimize the deviation from the target value.

6.4 Results and Discussion

6.4.1 Base Case

In this section, the results obtained from pre-emptive, non-preemptive, and weighted objective models are analyzed based on multiple criteria. The ideal and target values for the objective functions are presented in Table 6.1. The first goal constraint (G1) ensures that the total supply chain cost does not exceed $531,615. The second (G2) and third goals (G3) achieve a maximum value of 25,374 and 233 for the overall shortage and outdated units, respectively.

Table 6.1: Ideal and Target Values for the Three Objectives

	Ideal Value	**Target Value**
Cost	$506,300	$531,615
Units of Shortage	24,166	25,374
Units of Outdated	222	233

Table 6.2 showcases the results generated by the preemptive goal programming (PGP) model for the set precedence. As mentioned in the earlier section, total supply chain cost is assigned the highest priority, followed by unit shortage and unit outdated. It is observed that the model achieved the target value for the total costs but exceeded the unit shortage and outdated by 371% and 479%, respectively. Similarly, Table 6.3 displays the outcome from the non-preemptive goal programming (NPGP) model based on ideal value scaling. The weights assigned to the performance parameters in the base case of the current model are in the same order as the PGP model.

The aim of an NPGP model is to minimize the sum of weighted deviations from the assigned target value. However, despite setting a higher weight to the total SC cost, the model solution went beyond the desired value by over 120%. While the total shortage units also eclipsed the threshold level by over 420%, the model accomplished the specified value for the units outdated. The findings from the weighted objective method (WOM) follow a comparable trend with the NPGP model, with the supply chain cost and unit shortage surpassing the suggested value for the base case by 125% and 380%, respectively. On the other hand, the unit outdated yielded six units less when compared with the target value. The results obtained from the WOM are demonstrated in Table 6.4.

Table 6.2: Results from the Preemptive Goal Programming Model

Minimize Z= $P_1 d_1^+ + P_2 d_2^+ + P_3 d_3^+$	**Ideal Objective Value**	**Target Objective Value**	**Achieved Objective Value**	**Goal Achievement**	**Priorities**
Total Cost ($)	$506,300	$531,615	$531,615	Achieved	P1
Total Units of Shortage	24,166	25,374	89,601	Not Achieved (371%)	P2
Total Units of Outdated	222	233	1,064	Not Achieved (479%)	P3

Table 6.3: Results from the Non-Preemptive Goal Programming Model

Minimize Z= $\frac{w_1 d_1^+}{\gamma_1} + \frac{w_2 d_2^+}{\gamma_2} + \frac{w_3 d_3^+}{\gamma_3}$	**Ideal Objective Value**	**Target Objective Value**	**Achieved Objective Value**	**Goal Achievement**	**Weights**
Total Cost ($)	$506,300	$531,615	631,349	Not Achieved (125%)	0.5
Total Units of Shortage	24,166	25,374	102,944	Not Achieved (425%)	0.3
Total Units of Outdated	222	233	233	Achieved	0.2

Table 6.4: Results from the Weighted Objective Model Goal Programming Model

Minimize Z= $\frac{w_1 * TOTPHC}{\gamma_1} + \frac{w_2 * TOTSHORT}{\gamma_2} + \frac{w_3 * TOTPEXP}{\gamma_3}$	**Ideal Objective Value**	**Target Objective Value**	**Achieved Objective Value**	**Goal Achievement**	**Weights**
Total Cost ($)	$506,300	$531,615	$633,112	Not Achieved (125%)	0.5
Total Units of Shortage	24,166	25,374	94,080	Not Achieved (380%)	0.3
Total Units of Outdated	222	233	227	Achieved	0.2

Figures 6.1 and 6.2 show the results of comparison from multiple objective models.

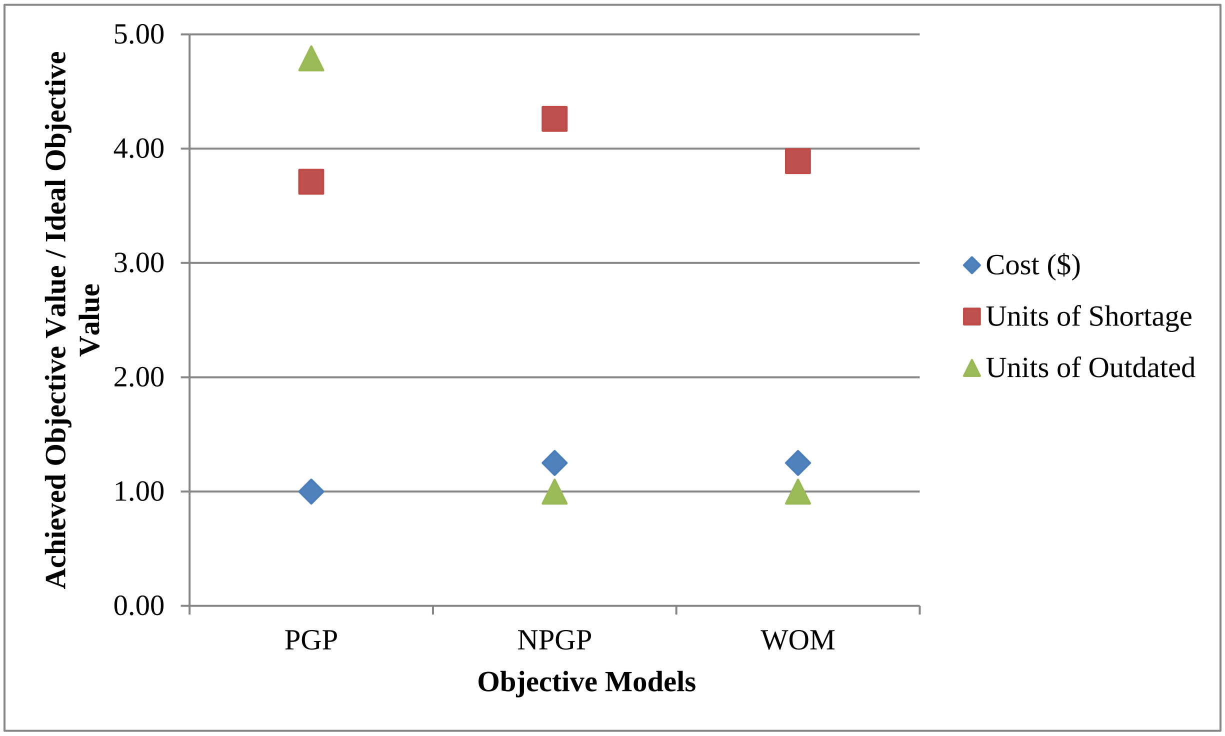


Figure 6.1: Comparison of Base Objective Results vs. Multiple Objective Models

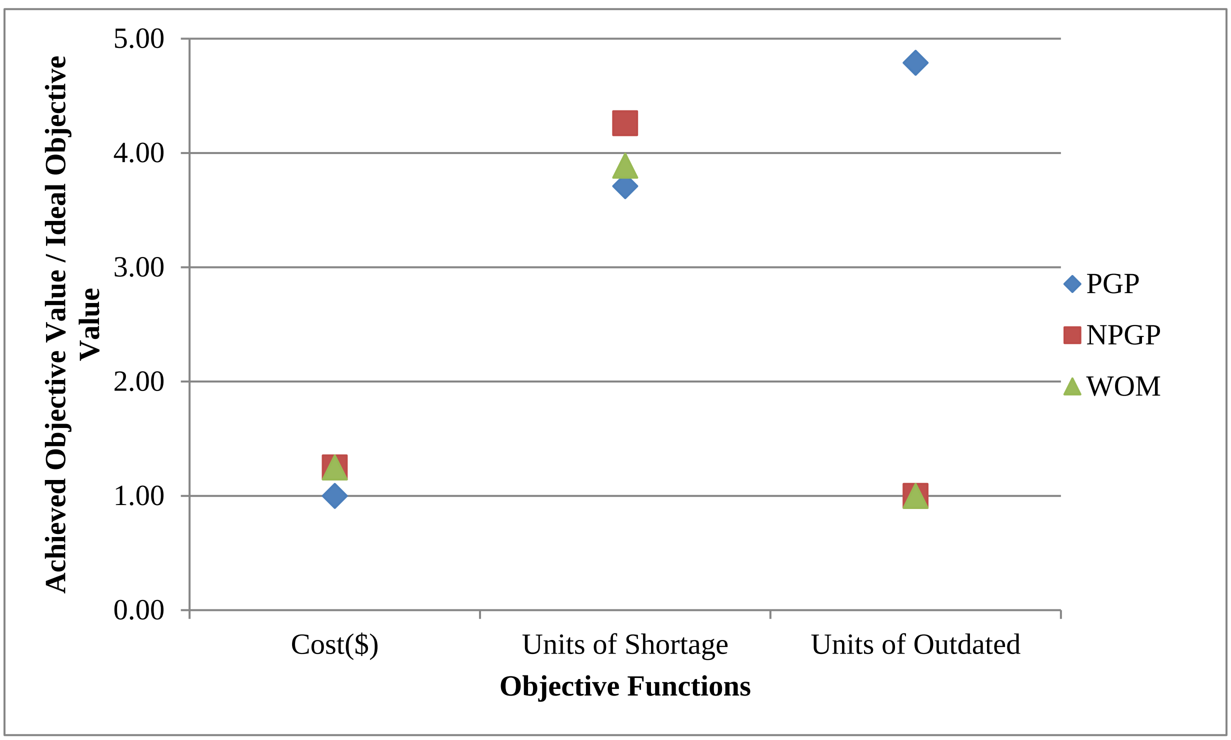


Figure 6.2: Comparison of Base Objective Results vs. Objective Functions

From the results of Figures 6.1 and 6.2 with base priorities, it is observed that

- On Preemptive Goal Programming (PGP) with P1 >> P2 >> P3, only the cost objective is achieved
- On Non-Preemptive Goal Programming (NPGP) with weight priorities = 0.5, 0.3, and 0.2, only the outdated objective is achieved
- On Weighted Objective Method (WOM) with weights = 0.5, 0.3, and 0.2, only the outdated objective is achieved
- The objective of total units of shortage is not achieved for three multiple objective models
- The three optimal solutions from the respective multiple objective models are non-dominated solutions. For instance, from the results, analyzing PGP and WOM solutions, a reduction in total outdated of 837 units (1,064 - 227) is achieved at a total cost increase of $101,497 ($633,112 - $531,615). Comparing NPGP and WOM solution, a reduction in total shortage of 8,864 units (102,944 - 94,080) is achieved at a total cost increase of $1,763 ($633,112-$631,349).
- In NPGP, its objective is to minimize the deviations from the target values. Minimizing the sum of weighted criteria in WOM is equivalent to minimizing the deviations from the target values. Thus, the WOM is basically similar to the NPGP technique.
- In Linear Programming, a linear program is infeasible if there exists no solution that satisfies all of the constraints -- in other words, if no feasible solution can be obtained. Goal Programming, which is similar to LP, may also have infeasible solutions. Our work in sensitivity analysis shows that there are infeasible solutions in scenarios 2, 3 and 5 under the Preemptive Goal Programming (PGP).
- The proposed three methods (Preemptive Goal Programming, Non Preemptive Goal Programming, and Weighted Objective Model) do not generally produce the same solutions. Because the three techniques entail distinct decision-making preferences, neither method, however, is superior to the other (Taha, 2017). Our works also demonstrate that neither method is superior to the other.

The impact of changing the importance order and weight priorities in the PGP, NPGP, and WOM model is discussed in the sensitivity analysis section.

6.4.2 Sensitivity Analysis

In this section, the influence of altering goal priorities in the PGP model and weights in the NPDP and WOM models are analyzed and discussed. Table 6.5 presents the results obtained from varying the priority order (P1, P2 and P3) of the three objective functions for the PGP model. It is interesting to note that the cost objective (G1) is only achieved when it has the highest priority. Similar performance of the model is noted between the Base case and scenario 1 with G1 being satisfied but units shortage and outdated exceeding the target value by approximately 370% and 470%, respectively. In scenario 4, the greatest priority is given to units outdated (G3) followed by supply chain cost and unit shortage. While the model accomplishes the desired value for G3, it surpasses the target value for G1 and G2 by over 120% and 370%, respectively. All other settings generated infeasible solutions. Therefore, changing the priority order of the objective functions did not have an impact on the solution except for scenario 4.

Table 6.5: Impact of Various Alternatives on the Respective Objective Functions under the Preemptive Goal Programming (PGP)

Scenarios	**Order of**	**Objective 1 IdealValue = $506,300**	**Objective 2 IdealValue =24,166**	**Objective 3 IdealValue =222**
	P1, P2, P3	**Cost ($)**	**Units Shortage**	**Units Outdated**
Base Case	P1 >> P2 >> P3	531,615 Achieved	89,601 Not Achieved	1,064 Not Achieved
Scenario 1	P1 >> P3 >> P2	531,615 Achieved	89,775 Not Achieved	1,045 Not Achieved
Scenario 2	P2 >> P1 >> P3	Infeasible Solution		
Scenario 3	P2 >> P3 >> P1	Infeasible Solution		
Scenario 4	P3 >> P1 >> P2	627,253 Not Achieved	89,479 Not Achieved	233 Achieved
Scenario 5	P3 >> P2 >> P1	Infeasible Solution		

As mentioned previously in the NPGP model, the supply chain cost is assigned the highest weight (0.5) in the base case, followed by units of shortage (0.3) and units of outdated (0.2). The variation in the allotted precedence of the three parameters in different scenarios along with the generated results, are showcased in Table 6.6. It is observed that G3 is completely achieved for all settings. However, similar to the base case, G1 and G2 are not satisfied for any scenario demonstrating that change in weights has no effect on the goal completion of the model. The greatest deviation in the supply chain cost is noted for scenarios 4 and 5. Similarly, the highest difference in units of shortage is seen in scenario 1. Interestingly, all other settings display a similar units of outdated value, whereas reducing the weights for G1 function resulted in an exponential increase in the supply chain cost.

Table 6.6: Impacts of Various Alternatives on the Objectives under Non-Preemptive Goal Programming (NPGP)

Alternate Scenario	**Weights**	**Objective 1 Ideal Value=$506,300**	**Objective 2 Ideal Value=24,166**	**Objective 3 Ideal Value=222**
		Cost ($)	**Units Shortage**	**Units Outdated**
Base Case	0.5,0.3,0.2	631,349 Not Achieved (125%)	102,944 Not Achieved (426%)	233 Achieved
Scenario 1	0.8,0.1,0.1	627,918 Not Achieved (134%)	101,755 Not Achieved (421%)	233 Achieved
Scenario 2	0.4,0.5,0.1	1.48171e7 Not Achieved (2,927%)	89,549 Not Achieved (371%)	233 Achieved
Scenario 3	0.4,0.1,0.5	1.48024e7 Not Achieved (2,923%)	89,515 Not Achieved (371%)	233 Achieved
Scenario 4	0.1,0.45,0.45	2.24393e7 Not Achieved (4,432%)	89,353 Not Achieved (362%)	233 Achieved
Scenario 5	0.3,0.3,0.4	2.24228e7 Not Achieved (4,429%)	89,382 Not Achieved (362%)	233 Achieved

An identical approach to varying weights of the three performance metrics in the previous model is applied for the weighted objective method model. Similar to the NPGP model, G1 and G2 are not achieved for any setting, and a reduction in the weight of the supply chain cost results in a significant deviation from the base case value as seen in scenarios 3 - 5. Furthermore, unit outdated objectives are achieved irrespective of weights in all the cases. It is interesting to note that all scenarios (except scenario 2) outperformed the base case for G3. The results obtained from the WOM model are presented in Table 6.7.

Table 6.7: Impacts of Various Alternatives on the Respective Objectives under Weighted Objective Method (WOM)

Alternate Scenarios	**Priorities**	**Objective 1 Ideal Value=$506,30**	**Objective 2 Ideal Value=24,166**	**Objective 3 Ideal Value=222**
		Cost ($)	**Units Shortage**	**Units Outdated**
Base Case	0.5,0.3,0.2	633,112 Not Achieved (125%)	94,080 Not Achieved (389%)	227 Achieved
Scenario 1	0.8,0.1,0.1	632,168 Not Achieved (112%)	91,951 Not Achieved (380%)	217 Achieved
Scenario 2	0.4,0.5,0.1	633,467 Not Achieved (112%)	92,018 Not Achieved (381%)	228 Achieved
Scenario 3	0.4,0.1,0.5	658,648 Not Achieved (130%)	94,330 Not Achieved (390%)	224 Achieved
Scenario 4	0.1,0.45,0.45	5.6912 e6 Not Achieved (1,124%)	92,134 Not Achieved (381%)	219 Achieved
Scenario 5	0.3,0.3,0.4	786,162 Not Achieved (155%)	96,657 Not Achieved (392%)	220 Achieved

CHAPTER 7
CONCLUSIONS AND FUTURE WORK

Supply chain management of blood and its products is of paramount importance in medical treatment due to its perishable nature, uncertain demand, and lack of auxiliary substitutes (Delen et al., 2011). For example, the Red Blood Cells (RBC's) have a life span of approximately 40 days, whereas platelets have a shelf life of up to five days after extraction from the human body (Arani et al., 2021). According to the World Health Organization, approximately 112 million blood units are collected worldwide annually. However, nearly 20% of units are discarded in developed nations due to expiry before the final use. A similar trend is noticed in developing countries as well. Therefore, managing blood distribution and developing an efficient network is considered a critical issue in the supply chain domain.

A standard blood supply chain (BSC) achieves the movement of blood products (red blood cells, white blood cells, and platelets) from initial collection to final patients in several echelons. The first step comprises of donation of blood by donors at the donation or mobile centers. The donation sites transport the blood units to blood centers where several tests for infections are carried out. The blood centers then store either the whole blood units or segregate them into their individual products. Finally, they are distributed to the healthcare facilities when required. In addition, blood supply forecasting is essential for making supply chain decisions, such as donor drive scheduling, vehicle routing policies, and inventory management, at blood centers and hospitals. Therefore, developing optimal ordering policies with the goal to minimize the outdating and shortage of platelets is very important.

This dissertation, firstly, aims to efficiently forecast the supply of blood components at blood centers, then with generated blood supply and demand distributions from historial data as inputs of blood supply chain, a single stochastic objective inventory model for two hospitals and one blood center is developed to determine the number of platelet units to order and time between orders under the supply and demand uncertainty. A case study is demonstrated incorporating this model. The model is continued to be developed to a stochastic inventory management tool for a divergent blood supply chain under the uncertainties of supply of blood and demand for blood. Furthermore, the basic stochastic blood management model for the hospitals and blood center is extended to a stochastic blood management model by considering multiple objectives.

7.1 Contributions of this Thesis

The main contributions of this thesis are theoretical contributions, methodological contributions and empirical contributions.

7.1.1 Theoretical Contributions

- The uncertainty in supply and perishable characteristics of blood products has led to a substantial outdating of the collected donor blood. On the other hand, due to the very limited donor population, hospitals and blood centers experience severe blood shortage. Therefore, the necessity to forecast the blood supply to minimize outdating as well as shortage is obvious. This thesis aims to efficiently forecast the supply of blood components at blood centers.
- The majority of research on blood inventory management assumed that the demand is deterministic (Dillon et al., 2017). However, it is essential to consider the uncertainty of blood demand (Haijema et al., 2007). The issues regarding inventory management are greatly complicated by unknown demand and make it challenging to render significant models in practice. A few recent researchers (Solyal et al., 2015; Fortsch and Khapalova, 2016; and Rajendran and Ravindran, 2017) address demand uncertainty issues in inventory management. There has been very little research work considering both supply and demand uncertainty. Blood inventory management needs to take the uncertainty aspect of blood supply and demand into account for the blood supply chain studied.
- Very limited previous work has been focused on blood inventory management for the entire blood supply chain. In Chapters 4, we have developed stochastic programming models under blood supply and demand uncertainty for determining the ordering policies for the entire blood supply chain with one blood center and two hospitals. Additionally, the models consider two types of demands requested from the hospitals to the blood center: *regular demand* and *emergency demand*. At the end of each day, hospitals placed the *regular demand* of blood to blood center and will be delivered to hospitals after the lead-time. The *emergency demand* of blood has to be supplied by the blood center to the hospital promptly. Furthermore, the stochastic inventory management models developed in Chapter 5 is one of the pioneer research work to incorporate the platelet inventory management for a divergent blood supply chain with two blood centers and four hospitals under supply and demand uncertainty.

7.1.2 Methodological Contributions

- Two different types of forecasting techniques, time series and machine learning algorithms, are developed and the best performing method for the given case study is determined. Autoregressive (AUTOREG), Autoregressive Moving Average (ARMA), Autoregressive Integrated Moving Average (ARIMA), Seasonal ARIMA, Seasonal Exponential Smoothing Method (ESM), and Holt-Winters models are considered under the time series. Artificial neural network (ANN) and multiple regression are considered under the machine learning algorithms.
- Due to the blood's perishable characteristics coupled with its supply and demand uncertainty, few studies have focused on its redistribution amongst the health care centers within the same geographical region (Dehghani et al., 2019; Denesiuk et al., 2006; Rajendran and Ravindran, 2019). However, the typical network they consider comprises of a single blood center, which supplies the blood products to multiple hospitals. The present investigation formulates a model for the blood supply chain with the objective of minimizing the overall cost incurred for the redistribution of blood in a network where multiple blood centers can supply the required amount to the medical facilities existing outside their usual network. Several parameters, such as unit purchasing, outdating, inventory, and transportation, are examined at the hospital as well as the blood center level.
- The majority of previous work on blood inventory management assumes the cost components can be measured associated with the entire blood supply chain (Haijema, 2007; Haijema, 2009; van Dijk, 2009; Gunpinar and Centeno, 2015; Rajendran and Ravindran, 2017, 2019). In reality, some cost elements cannot be measured in the same units accurately, such as shortage cost and outdated cost. In this dissertation, multiple criteria mathematical programming (MCMP) models considering conflicting criteria such as the amount of outdating and shortage, holding cost and ordering cost for platelet inventory management have been developed and solved using three techniques– preemptive goal programming, non-preemptive goal programming and weighted objective method. From the results of the three MCMP techniques and operational settings, the hospital management is able to decide the amount of how many platelets to purchase.

7.1.3 Empirical Contributions

The inventory management considered in this work will be one of the first recommended systems to determine blood order quantity at blood banks and blood centers based on historical supply and demand data. Past research has proven that developing proper inventory models will result in millions of dollars of savings to blood banks and blood centers, and hence, the proposed work is developed to carry out as a decision support system so that pathologists at blood banks, blood centers and hospitals can make decisions determining the number of units to purchase and time between orders. Upon implementation of the models, it can help Taiwan Blood Services Foundation and other health care professionals manage and control blood inventory more effectively under blood supply and demand uncertainty, thus decreasing the shortage of blood and expired wastage of blood.

This thesis also elaborated the following empirical results for the blood inventory management in blood supply chain:

- **Gathered five years' worth of historical blood supply data from Taiwan Blood Services Foundation (TBSF) to conduct the forecasting**

  We have interacted with TBSF on the collaborative research and gathered five years' worth of historical blood supply data. On comparing the different techniques, it is found that time series forecasting methods yield better results than machine learning algorithms. More specifically, the least value of the error measures are observed in seasonal ESM and ARIMA models

- **Manage the blood supply chain more effectively under the demand and supply uncertainty**

  We propose an essential blood supply chain model with emphasis on how to manage the blood supply chain under the uncertainty of demand and supply more effectively. Furthermore, this study conducted a sensitivity analysis to examine the impacts of the coefficient of demand and supply variation (please refer to table 4.3 in chapter 4) and the cost parameters (please refer to table 4.6 in chapter 4) on the average total cost and the performance measures (units of shortage, outdated units, inventory holding units, and purchased units) for both the blood center and hospitals. Based on the results, the hospitals and the blood center can choose the optimal ordering policy that works best for them. From the results, we observed that when the coefficient of demand and supply variation is increased, the expected supply chain cost increased with more outdating units, shortages units, and holding units due to the impacts of supply and demand fluctuation. Variation in the inventory holding and expiration costs has an insignificant effect on the total cost. The model developed in this paper can assist managers and pathologists at the blood donation centers and hospitals to determine the most efficient inventory policy with a minimum cost based on the uncertainty of blood supply and demand.

Weekday Implementation Results of Case Study

In chapter 4, the model is solved with one blood center and two hospitals for a planning horizon frame of 300 days and 100 scenarios. In practice, the same order policy may not be used for all the 300 days of the planning horizon. Instead, a rolling horizon approach may be followed to implement the optimal solution. At the end of the first week, the MILP model is returned for the next 300 days after updating the inventory and demand forecast. The new optimal policy will be used for the second week, and the process is repeated weekly. Since long-term forecasts may not be as good as short-term forecasts, a rolling horizon policy helps to update forecasts weekly and determine the best solution based on the revised forecasts.

The case study implemented in this chapter is focused on weekday blood ordering for one blood center and two hospitals based on the assumption that the weekday demand/supply are normal distributions with various means (please refer to table 4.12 in chapter 4). From the results, it is shown that the units purchased, outdated, held in inventory, and shortage varied with the inflation in the demand and supply, and the average total supply chain cost varied with the inflation in the demand and supply

Divergent Blood Supply Chain under Supply and Demand Uncertainty

While previous studies on blood supply chain management focus on a single blood center and a multiple hospitals system with the objective to minimize the total supply chain cost (consisting of transportation, purchasing, shortage, outdating, and inventory costs). The practical contribution of the present study is to determine the optimal ordering policy for a divergent network consisting of multiple blood centers and hospitals. Sensitivity analysis is conducted to understand the influence of the supply and demand variation, as well as the cost parameters. The results indicate that a change in the mean demand has a linear impact on the supply chain cost, whereas the mean supply has a minimal impact on the total cost parameter. Furthermore, an increase in the coefficient of demand variation induces a rise in the total supply chain by 5.55%, while a 4.8% increase is observed when varying the coefficient of supply variation parameter. The present study investigates the impact of four hospitals and two blood centers and the model examined the results for nine different demand settings (please refer to table 5.3 in chapter 5) and five distinct supply settings (please refer to table 5.5 in chapter 5).

It is observed that four demand settings (DS 3, 5, 7, and 9) displayed a lower average cost per day per scenario when compared to the base case. At the blood center level, a rise in cost was seen for variation in supply settings causing fluctuations in the units outdating. This thesis also conducted sensitivity analysis by varying supply and demand along with the cost variation. The results demonstrate a significant deviation for the inventory level at the hospitals and blood centers, which leads to a higher average cost in the supply chain. An insignificant change is evident in the shortage and outdating cost for different cost variation settings. Based on the results, the model is robust for all settings and can easily be extended to include more sites in the supply chain. Procuring emergency units from other blood centers to compensate for shortages and reduce unit outdating would improve the functionality of the system and prevent hundreds of surgeries from being canceled each day. The developed framework in the present study can be easily extended for other similar supply chains having unpredictable supply and demand and deals with perishable products.

7.2 Directions of Future Research

The following are the potential future work:

- **Blood Supply Chain During a Pandemic Outbreak**

  The COVID-19 pandemic has caused unprecedented challenges to the U.S. blood supply. Donor centers have experienced a dramatic reduction in donations due to the implementation of social distancing and the cancellation of blood drives (Ngo et al., 2020; https://www.fda.gov). COVID-19 has had a negative impact on blood collection. Furthermore, all the elective surgeries and non-urgent clinical interventions have also been postponed during this time. This has led to a drop in blood collection, demand as well as the issue at the blood center (Raturi and Kusum, 2020). Blood supply chain management during the pandemic has become more important than before. To transition back to the normal conditions, it would most likely depend on the extent and the time duration of this pandemic and associated behavioral changes (Raturia and Kusumb, 2020). It is necessary to do future research to address the impact of next pandemic on the blood inventory management and develop effective strategies for blood collection and optimization of the blood supply chain during the next pandemic.

- **Blood Substitution for Supply Chain**

  Regarding blood transfusions, matching blood types is the process for compatibility testing between the donor's blood and the blood of the recipient. Cross-matching generally does not mean an identical blood match. Duan and Liao (2014) shows a table regarding the distribution of red blood cell types and all possible suitable substitutions for ABO/Rh (D) in the US Population and investigate an ABO compatible substitution scenario at both hospital and blood center by proposing a simulation optimization (SO) approach. Further research is encouraged.

- **Vehicle Routing Policies for Blood Supply Chain**

  There are two main vehicle routing operations in the blood supply chain management: (i) distribution of donated blood from the donation stations to blood centers, and (ii) distribution of blood products from blood centers to hospitals. Because the collected blood has to be transferred to the blood center within 4-6 hours of collection. Therefore, the processing time limit forces the organizations to schedule multiple pickups from the donation sites and efficiently transferred them to the blood center. The other routing operation deals with the delivery of blood components from blood centers to hospitals. Some situations require that blood components to be transported far away from the blood centers to hospitals, and hence, it is crucial to schedule efficient vehicle routings in order to reduce the overall transportation cost.

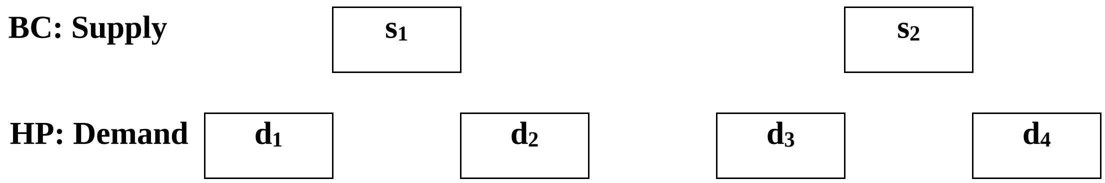
- **Drone Delivery for the Blood Products**

  To study the vehicle routing policies for blood products in supply chain, one alternative is to evaluate the drone delivery for blood products. Remote technology and automation have been present for centuries, giving human operators safety from harm and enabling new task functionality. Autonomous unmanned aerial vehicles (UAVs) technology has progressed in recent years, potential use case for UAVs (Glauser, 2018; Haidari et al., 2016; Goodchild and Toy, 2018) have received considerable attention from researchers (Gilmore et al., 2019; Merkert and Bushell, 2020) due to their ability to travel difficult terrains, and replace fleet for vehicles that require costly maintenance. Several companies have recognized the benefits of using drones for blood product delivery (Ling and Draghic, 2019). It is necessary to do research furthermore to examine the impact of drone delivery on the overall supply chain cost.

- **Closed-Loop Blood Supply Chain**

  A closed-loop supply chain essentially considers forward and reverse supply chains simultaneously (Govindan, Soleimani and Kannan, 2015). Blood with false-negative bacterial contamination or when excess units are ordered could be sent back to blood centers with reusable possibilities. In these cases, the cost associated with reverse shipment has to be considered in the model. However, none of the previous research takes the reverse shipment cost and the associated changes in inventory into consideration.

APPENDIX: Centralized Blood Supply Chain vs. Decentralized Blood Supply Chain



A centralized blood supply chain is better than decentralized blood supply chain

<u>Proof:</u> Assume a supply chain consisting of s_i blood centers and d_j hospitals.

Consider a system having two blood centers and four hospitals with blood center s_1 supplying platelet units to hospital $d_1$and d_2 while blood center s_2 supplying platelet units to hospitals d_3 and d_4.

In a centralized supply chain, the difference between total supply and total demand is zero if there is are no shortage and outdated units, i.e. $(s_1 + s_2) - (d_1 + d_2 + d_3 + d_4) = 0$. If the difference is greater than zero, then the system would have units outdated, whereas the supply chain would experience shortage if the difference is less than zero.

In a decentralized system, the difference between supply and demand from blood center s_1 is $s_1 - (d_1 + d_2)$. Similarly, the difference between supply and demand from blood center s_2 is $s_2 - (d_3 + d_4)$. We will consider the following cases:

<u>Case 1</u>: If $s_1 - (d_1 + d_2) \geq 0$ and $s_2 - (d_3 + d_4) \geq 0$, then outdating exists at blood centers s_1 and s_2 and the performance of a centralized supply chain would be equal to a decentralized system.

<u>Case 2</u>: If $s_1 - (d_1 + d_2) < 0$ and $s_2 - (d_3 + d_4) < 0$, then there is a shortage of platelet units at the blood centers s_1 and s_2 and the performance of a centralized supply chain would be equal to a decentralized system.

<u>Case 3</u>: If $s_1 - (d_1 + d_2) > 0$ and $s_2 - (d_3 + d_4) < 0$, then the supply chain would experience outdating at blood center s_1 and shortage at blood center s_2. Adding the two scenarios we get, $(s_1 + s_2) - (d_1 + d_2 + d_3 + d_4)$, which is either going to be greater than zero or less than zero. The former case would indicate that the supply chain has units outdating. However, that would be less when compared to the units outdating achieved in a decentralized system ($s_1 - (d_1 + d_2)$). Similarly, the latter case would indicate that the supply chain has a shortage, which would be less when compared to the shortage experienced in the decentralized system ($s_2 - (d_3 + d_4)$). Therefore, a centralized system would be better than a decentralized system.

<u>Case 4</u>: If $s_1 - (d_1 + d_2) < 0$ and $s_2 - (d_3 + d_4) > 0$, then the supply chain would experience shortage at blood center s_1 and outdating at blood center s_2. Adding the two scenarios we get, $(s_1 + s_2) - (d_1 + d_2 + d_3 + d_4)$, which is either going to be greater than zero or less

than zero. The former case would indicate that the supply chain has units outdating. However, that would be less when compared to the units outdating achieved in a decentralized system ($s_2 - (d_3 + d_4)$). Similarly, the latter case would indicate that the supply chain has a shortage, which would be less when compared to the shortage experienced in the decentralized system ($s_1 - (d_1 + d_2)$). Therefore, a centralized system would be better than a decentralized system.

Thus, for all possible cases, we can conclude that a centralized system is better than a decentralized system in the blood supply chain.

BIBLIOGRAPHY

Abbasi, B., and Hosseinifard, S.Z. (2014) 'On the Issuing Policies for Perishable Items such as Red Blood Cells and Platelets in Blood Service', Decision Sciences, 45(5).

Abolghasemi, H., Radfar, M.H., Tabatabaee, M., Hosseini-Divkolay, N. S., and Burkle, F. M. (2008). 'Revisiting blood transfusion preparedness: experience from the Bam earthquake response', Prehospital and disaster medicine, 23(05), 391-394.

Albdulwahab, US (2015) 'Blood Platelet Bank Inventory Management: An Approximate Dynamic Programming Approach', Ph.D. Dissertation, Ryerson University, Toronto, Ontario, Canada.

American Association of Blood Banks, (2007) 'National blood collection and utilization survey', extracted from http://www.aabb.org

American Association of Blood Banks, (2018) 'Blood FAQ', extracted from http://www.aabb.org

American Production and Inventory Control Society (APICS). (2016) 'Supply chain management (SCM) Dictionary', retrieved 2016-07-19.

American Red Cross. *Blood Types*. https://www.redcrossblood.org/learn-about-blood/ blood-types.html. Retrieved 15 July 2018.

American Red Cross. (2018) 'Red-Cross-issues-urgent-call-for-blood-donations-following-severe-winter-weather', http://www.redcross.org/news/press-release/Red-Cross-issues-urgent-call-for-blood-donations-following-severe-winter-weather

American Society of Hematology. *Blood Basics*. http://www.hematology.org/Patients/ Basics. Retrieved 20 July 2018.

Attari, M.Y.N., Pasandideh, S.H.R., Aghaie, A., and Niaki, S.T.A. (2017) 'Presenting a Stochastic multi-choice goal programming model for reducing wastages and shortages of blood products at hospitals', Journal of Industrial and Systems Engineering,10, special issue on healthcare, 81-96.

Beliën, J. and Forcé, H. (2012) 'Supply chain management of blood products: A literature review', European Journal of Operational Research, 217, 1-16.

Blackburn, J. and Scudder, G. (2009) 'Supply Chain Strategies for Perishable Products: The Case of Fresh Produce', Production and Operations Management, 18(2), 129–137.

Blake, J.T. (2009) ‘On the use of operational research for managing platelet inventory and ordering’, Transfusion, 49(3), 396-401.

Blood Donation Services in Taiwan. http://intra.blood.org.tw/upload/ce805c8a-9f64-45e3-ab07-20673a31164c.pdf. Retrived 12 August 2019.

Blood: the basics (2017) https://professionaleducation.blood.ca/en/transfusion/publications/blood-basics

Boppana, R.V., and Chalasani, S. (2007) ‘Analytical Models to Determine Desirable Blood Acquisition Rates’, In 2007 IEEE International Conference on System of Systems Engineering, San Antonio, TX.

Bosnes, V., Aldrin, M., Heier, H.E. (2005) ‘Predicting blood donor arrival’, Transfusion, 45(2), p. 162-170. https://www.ncbi.nlm.nih.gov/pubmed/15660823.

Box, G. E. P., Jenkins, G. M, and Reinsel, G. C. (2008) ‘Time series analysis forecasting and control’, Wiley Series.

Brodheim, E., Hirsch, R., Prastacos, G. (1976) ‘Setting inventory levels for hospital blood banks’, Transfusion 16(1), 63–70.

Butch, S.H. MA, MT (ASCP) SBB. (1985) ‘Blood Inventory Management’, Laboratory Medicine, 16(1).

Chopra, S. and Meindl, P. (2007) ‘Supply Chain Management- Strategy, Planning, and Operation’, Pearson Education, Inc., third edition.

Chopra, S., and P. Meindl, P. (2015) ‘Supply Chain Management: Strategy, Planning, and Operation’, 6th edition, Pearson-Prentice Hall.

Civelek, I., Karaesmen, I., & Scheller-Wolf, A. (2015). Blood platelet inventory management with protection levels. *European Journal of Operational Research*, *243*(3), 826-838.

Critchfield, G.C., Connelly, D.P., Ziehwein, M.S., Olesen, L.S., Nelson, C.E., Scott, E.P. (1985) ‘Automatic prediction of platelet utilization by time series analysis in a large tertiary care hospital’, American Journal of Clinical Pathology, 85(5), 627-631.

Cumming, P.D., Kendall, K.E., Pegels, C.C., Seagle, J.P., Shubsda, J.F. (1976) ‘A collections planning model for regional blood suppliers: description and validation’, Management Science 22, (9), 962–971.

Davey, R.J. (2004) ‘Recruiting blood donors: challenges and opportunities’. Transfusion 44(4): 597–600.

Denesiuk, L., Richardson, T., Nahirniak, S., Clarke, G. (2006) ‘Implementation of a redistribution system for near-outdate red blood cell units’, Archives of Pathology & Laboratory Medicine’, 130(8), 1178-1183.

Dillon, M., Oliveira, F., Abbasi, B. (2017) ‘A two-stage stochastic programming model for inventory management in the blood supply chain’, Int. J. Production Economics, 187, 27-41.

Duan, Q. and Liao, T.W. (2014) ‘Optimization of blood supply chain with shortened shelf lives and ABO compatibility’, Int. J. Production Economics, 153, 113-129.

Dumas, M.B., Rabinowitz, M. (1977) ‘Policies for reducing blood wastage in hospital blood banks’, Management Science, 23(10), 1124–1132.

Ekici, A., Özener, O. Ö, and Çoban, E. (2017) ‘Blood Supply Chain Management and Future Research Opportunities’, Operations Research Applications in Health Care Management, 241-266.

Ellingson, K.D., Sapiano, M.R.P., Haass, K.A., Savinkina, A.A., Baker, M.L., Chung, K.W., Henry, R.A., Berger, J.J., Kuehnert, M., and Basavaraju, S.V. (2017) ‘Continued decline in blood collection and transfusion in the United States–2015’, Transfusion, 57(2): 1588–1598.

Erickson, M.L., Champion, M.H., Klein, R. Ross, R.L., Neal, Z.M., Snyder, E.L. (2008), ‘Management of blood shortages in a tertiary care academic medical center: the Yale-New Haven Hospital frozen blood reserve’, Transfusion, 48(10), 2252-2263.

Fahimnia, B., Jabbarzadeh, A., Ghavamifar, A., and Bell, M. (2017) ‘Supply chain design for efficient and effective blood supply in disasters’, Int. J. Production Economics, 183, 700-709.

Federgruen, A., Prastacos, G.P., Zipkin, P.H. (1986) ‘An allocation and distribution model for perishable products’, Operations Research, 34(1), 75-82.

Filho, O.S., Cezarino, W., and Salviano, G.R. (2012) ‘A Decision-making Tool for Demand Forecasting of Blood Components’, Proceedings of the 14th IFAC Symposium on Information Control Problems in Manufacturing Bucharest, Romania.

Filho, O.S., Carvalho, M.A., Cezarino, W., Silva, R., and Salviano, G. (2013) ‘Demand Forecasting for Blood Components Distribution of a Blood Supply Chain’, 6th IFAC Conference on Management and Control of Production and Logistics, the International Federation of Automatic Control, Fortaleza, Brazil.

Fontaine, M.J., Chung, Y.T., Rogers, W.M., Sussmann, H.D., Quach, P., Galel, S.A., Goodnough, L.T.; Erhun, F. (2009) ‘Improving platelet supply chains through collaborations between blood centers and transfusion services’, Transfusion, 49(10), 2040-2047.

Fortsch, S.M. and Khapalova, E.A (2016) ‘Reducing uncertainty in demand for blood’, Operations Research for Health Care, 9, 16-28.

Frances, P.H. (2011) “Averaging model forecasts and expert forecasts: why does it work,” Interface, 41(2), 177-181.

Frankfurter, G. M., Kendall, K.E., Pegels, C. C. (1974) ‘Management Control of Blood through Short-Term Supply-Demand Forecast System’, Management Science, 21(4), 444-452.

Fries, B.E. (1975) ‘Optimal Ordering Policy for a Perishable Commodity with Fixed Lifetime’, Operations Research, 23(1), 46-61.

Gahirwal, M., and Vijayalakshmi, M. ‘Inter Time Series Sales Forecasting’, *Society‘s Institute of Technology*, Chembur, 2013, India. https://arxiv.org/abs/1303.0117

Gardner, Jr., E. S. (1990) ‘Evaluating Forecast Performance in an Inventory Control System’, Management Science, 36(4), 490-499.

Gerberding, J.L., Falk, H. Arias, I., Hunt, R.C. (2007) ‘In a Moment's Notice: Surge Capacity for Terrorist Bombings’, US Department of Health and Human Sciences, Atlanta, Georgia.

Ghandforoush, P. and Sen, T.K. (2010) ‘A DSS to manage platelet production supply chain for regional blood centers’, Decision Support Systems, 50(1), 32-42.

Glasgow, S. M., Allard, S., Doughty, H., Spreadborough, P., and Watkins, E. (2012) ‘Blood and Bombs: The Demand and Use of Blood Following the London Bombings of 7 July 2005– A Retrospective Review,’ Transfusion Medicine, 22(4), 244–250.

Govindan, K., Soleimani, H., and Kannan, D (2015) ‘Reverse logistics and closed-loop supply chain: A comprehensive review to explore the future,’ European Journal of Operational Research, 240, 603-626.

Gregor, P.J, Forthofer, R.N., Kapadia, A.S. (1982) 'An evaluation of inventory and transportation policies of a regional blood distribution system', European Journal of Operational Research, 10(1), 106–113.

Gunpinar, S. (2013) 'Supply Chain Optimization of Blood Products', Graduate Theses and Dissertations, Scholar Commons, University of South Florida.

Gunpinar S., Centeno, G. (2015) 'Stochastic integer programming models for reducing wastages and shortages of blood products at hospitals', Computers & Operations Research, 54, 129-141.

Haijema, R., van der Wal, J., van Dijk, N.M. (2007) 'Blood platelet production: optimization by dynamic programming and simulation', Computer & Oper Res 34(3), 760-779.

Haijema, R., van Dijk, N.M., van der Wal, J., Sibinga, C.S. (2009) 'Blood platelet production with breaks: optimization by SDP and simulation', International Journal of Production Economics, 121(2), 464-473.

Haijema, R. (2011) 'Optimal Issuing of Perishables with a Short Fixed Shelf Life', International Conference on Computational Logistics, Computational Logistics, 160-169.

Haijema, R., (2013) 'A New Class of Stock-level Dependent Ordering Policies for Perishables with a Short Maximum Shelf Life', International Journal of Production Economics, 143(2), 434-439.

Heddle, N.M., Liu, Y., Barty, R., Webert, K.E., Whittaker, S., Gagliardi, K., Lauzon, D., Owens, W. (2009) 'Factors affecting the frequency of red blood cell outdates: an approach to establish benchmarking targets', Transfusion, 49(2), 219-226.

Hemmelmayr, V., Doerner, K.F., Hartl, R.F., and Savelsbergh, M.W.P. (2010) 'Vendor managed inventory for environments with stochastic product usage', European Journal of Operational Research, 202(3), 686-695.

Hemmelmayr, V., Doerner, K.F., Hartl, R.F., and Savelsbergh, M.W.P. (2009) 'Delivery strategies for blood products supplies', OR Spectrum 31(4), 707–725.

Heydari, J., Kazemzadeh, R.B., and Chaharsooghi, S.K. (2009) 'A study of lead time variation impact on supply chain performance', Int J Adv Manuf Technol, 40:1206–1215

Hyndman, R. J., and Thanasopoulos, G. (2018) *Forecasting: principles and practice*, OTexts, 2nd edition.

Jabbarzadeh, A., Fahimnia, B., & Seuring, S. (2014) ‘Dynamic supply chain network design for the supply of blood in disasters: A robust model with real world application’, Transportation Research Part E: Logistics and Transportation Review, 70, 225-244.

Jagannathan, R. and Sen, T. (1991) ‘Storing crossmatched blood: a perishable inventory model with prior allocation’, Management Science, 37(3), 251–266.

Jennings, J.B. (1973) ‘Blood Bank Inventory Control’, Management Science, 19(6), 637-645.

Jones, D. and Tamiz, M. (2010) ‘Practical Goal Programming’, International Series in Operations Research and Management Science, Springer

Kamp, C., Heiden, M., Henseler, O., Seitz, R. (2010) ‘Management of blood supplies during an influenza pandemic’, Transfusion, 50(1).

Katsaliaki, K., Brailsford, S.C. (2007) ‘Using simulation to improve the blood supply chain’, Journal of the Operational Research Society, 58(2), 219-227.

Katsaliaki, K. (2008) ‘Cost-effective practices in the blood service sector’, Health Policy, 86, 276-287.

Katz, A.J., Carter, C.W., Saxton, P., Blutt, J., Kakaiya, R.M. (1983) ‘Simulation analysis of platelet production and inventory management’, VoxSanguinis, 44(1), 31-36.

Kelleher, J.D., Namee, B.M., and D'Arcy, A. (2015) ‘Fundamentals of Machine Learning for Predictive Data Analytics: Algorithms, Worked Examples, and Case Studies’, The MIT Press, 1st Edition.

Kendall, K.E. (1980) ‘Multiple objective planning for regional blood centers’, Long Range Planning’, 13(4), 98-104.

Kendall, K.E. (1980) ‘Formulating blood rotation policies with multiple objectives’, Management Science, 26(11), 1145-1157.

Khanghahi, M. E., Moghaddam, R.T., Taleizadeh, A.A., and Amin, S.H. (2018) ‘Designing and optimizing a sustainable supply chain network for a blood platelet bank under uncertainty’, Engineering Applications of Artificial Intelligence, 71, 236-250.

Khaldi, R., Afia, A.E., Chiheb, R., and Faizi, R. (2017) ‘Artificial Neural Network Based Approach for Blood Demand Forecasting: Fez Transfusion Blood Center Case’, Mohammed V University.

Kopach, R. (2008) ‘Tutorial on constructing a red blood cell inventory management system with two demand rates’, European Journal of Operational Research, 185(3), 1051-1059.

Ledman, R.E., Groh, N. (1984) ‘Platelet production planning to ensure availability while minimizing outdating’, Transfusion, 24(6), 532-533.

Lestari, F., Anwar, U., Nugraha, N., and Azwar, B., (2017), ‘Forecasting Demand in Blood Supply Chain (Case Study on Blood Transfusion Unit)’, Proceedings of the World Congress on Engineering, Vol II, London, U.K.

Li, Z., Fei, W., Zhou, E., Gajpal, Y., and Chen, X., (2019), ‘The Impact of Lead Time Uncertainty on Supply Chain Performance Considering Carbon Cost’, Sustainability, 11(22): 6457

Liu, L. and Lian, Z. (1999) ‘(s, S) Continuous Review Models for Products with Fixed Lifetimes’ Operations Research, 47(1), 150-158.

Lowalekar, H. and Ravichandran, N. (2015) ‘Chapter 18: Inventory Management in Blood Banks’, Operations Management and Quantitative Techniques Area, Indian Institute of Management Indore.

Mansur, A., Vanany, I., and Arvitrida, N.I. (2018) ‘Challenge and opportunity research in blood supply chain management: a literature review’, MATEC Web of Conferences 154, 01092.

Michaels, J.D., Brennan, J.E., Golden, B.L., Fu, M.C. (1993) ‘A simulation study of donor scheduling systems for the American Red Cross’, Computers & Operations Research, 20(2), 199-213.

Montgomery, D.C., Jennings, C.L., and Kulahci, M., (2008) Introduction to Time Series Analysis and Forecasting, John Wiley & Sons, Inc.

Mulcahy, A.W., Kapinos, K.A., Briscombe, B., Uscher-Pines, L., Chaturvedi, R., Case, S.R., Hlávka, J., and Miller, B.M., (2016) ‘Toward a Sustainable Blood Supply in the United States- An Analysis of the Current System and Alternatives for the future’, extracted from Rand Corporation, https://www.rand.org/

Muriana, C. (2016) ‘An EOQ model for perishable products with fixed shelf life under stochastic demand conditions’, European Journal of Operational Research, 255, 388-396.

Nahmias, S and Pierskalla W.P. (1973) ‘Optimal ordering policies for a product that perishes in two periods subject to stochastic demand’, Naval research logistics quarterly, 20(2), 207-229.

Nahmias S. (1975) ‘Optimal Ordering Policies for Perishable Inventory-II’, Operations Research, 23(4), 735-749.

Nahmias, S. (1982) ‘Perishable inventory theory: a review’, Operations research, 30(4), 680-780.

Nahmias, S. (2015) *Production and operations analysis: strategy, quality, analytics, application,* Long Grove, Illinois: Waveland Press, Inc.

Nagurney, A. (2006) ‘Supply Chain Network Economics: Dynamics of Prices, Flows, and Profits’, Edward Elgar Publishing, Cheltenham, England.

Nagurney, A. (2012) ‘Operations Management and Supply Chain Network Theory’, University of Gothenburg Fall 2012 PhD Course.

Nagurney, A. (2017) ‘Uncertainty in blood supply chains creating challenges for industry’, extracted from https://www.informs.org; https://theconversation.com/uncertainty-in-blood-supply-chains-creating-challenges-for-industry.

Nagurney, A., Masoumi, A.H., and Yu, M. (2012) ‘Supply Chain Network Operations Management of a Blood Banking System with Cost and Risk Minimization’, Computational Management Science, 9(2), 205-231.

Najafi, M., Ahmadi, A., and Zolfagharinia, H. (2017) ‘Blood inventory management in hospitals: considering supply and demand uncertainty and blood transshipment possibility’, Operations Research for Health Care, 15, 43-56.

National Blood Centers, (2004). ‘Comprehensive Report on Blood Collection and Transfusion in the United States in 2001. Technical report’, National Blood Data Resource Center, Bethesda, MD.

National Heart, Lung, and Blood Institute. (2018) ‘blood-transfusion’, https://www.nhlbi.nih.gov/health-topics/blood-transfusion

Niknam, T., Abarghooee, R.A., and Narimani, M.R. (2012) ‘An efficient scenario-based stochastic programming framework for multi-objective optimal micro-grid operation’, Applied Energy, 99, 455-470

Nollet, K. E., Ohto, H., Yasuda, H., and Hasegawa, A. (2013) ‘The great East Japan earthquake of March 11, 2011, from the vantage point of blood banking and transfusion medicine’, Transfusion medicine reviews, 27(1), 29-35.

Osorio, A.F., Brailsford, S.C., and Smith, H.K. (2015) ‘A structured review of quantitative models in the blood supply chain: a taxonomic framework for decision-making’, International Journal of Production Research, 53(24), 7191–7212.

Pankratz, A. (1983) *Forecasting with Univariate Box-Jenkins Models: Concepts and Cases*. New York: John Wiley & Sons.

Pauls-Worm, K.G.J., and Hendrix, E.M.T. (2018) 'Inventory control for a non-stationary demand perishable product: comparing policies and solution methods', Operations Research and Logistics, Wageningen University, orcid; Computer Architecture, Universidad de Málaga, orcid.

Pereira, A. (2004) 'Performance of time-series methods in forecasting the demand for red blood cells transfusion', Transfusion, Vol. 44, 739-746

Pereira, A. (2005) 'Blood inventory management in the type and screen era', VoxSanguinis, 89(4), 245-250.

Perera, G., Hyam, C., Taylor, C., Chapman, J., (2009) 'Hospital Blood Inventory Practice: the factors affecting stock level and wastage', Transfusion Medicine, Blood Stocks Management Scheme, 19, 99-104.

Pierskalla, W. P., Sassetti, R.J., Cohen, M.A. (1980) "Regionalization of Blood Banking Services, In Executive Summary', edited by The Wharton School of the University of Pennsylvania, Philadelphia, 1–29. Philadelphia, PA: University of Pennsylvania.

Pierskalla, W.P. (2005), 'Supply chain management of blood banks' from 'Operations research and health care: A handbook of methods and applications', USA: Kluwer Academic Publishers, Chapter 5, 103-145.

Pink, J., Thomson, A., Wylie, B. (1994) 'Inventory management in Sydney-Public-Hospital blood banks', Transfusion Medicine, 4,(3), 237-242.

Prastacos, G.P. (1978) 'Optimal myopic allocation of a product with fixed lifetime', J Oper Res Soc 29(9), 905–913.

Prastacos, G.P. (1981) 'Allocation of a perishable product inventory', Oper Res 29(1), 95–107.

Prastacos, G.P. (1984) 'Blood Inventory Management: An Overview of Theory and Practice', Management Science, 30(7), 777-800.

Prastacos, G.P., Brodheim, E. (1980) 'PBDS: a decision support system for regional blood management', Management Science, 26(5), 451-463.

Quillen, K. and Luckey, C. J. (2014) 'Blood and Bombs: Blood Use After the Boston Marathon Bombing of April 15, 2013', Transfusion, 54(4), 1202–1203.

Rajendran, S. (2013) ‘Inventory Management At Hospitals To Minimize Platelet Wastage’, Master Thesis, Industrial Engineering, The Pennsylvania State University.

Rajendran, S. (2016) ‘Finite and infinite time horizon inventory models to minimize platelet wastage at hospitals’, International Journal of Operations and Quantitative Management, 22(2), 119–140.

Rajendran, S. and Ravindran, A.R. (2017) ‘Platelet ordering policies at hospitals using stochastic Integer programming model and heuristic approaches to reduce wastage’, Computers & Industrial Engineering, 110, 151-164.

Rajendran, S. and Ravindran, A.R. (2019) ‘Inventory management of platelets along with blood supply chain to minimize wastage and shortage’, Computers & Industrial Engineering, 130, 714-730.

Ravindran, A. (2008) *Operations Research and Management Science Handbook,* CRC Press.

Ravindran, A., and Warsing, D.P. (2013) *Supply Chain Engineering: Models and Applications,* CRC Press.

Rytilä, J.S. and Spens, K.M. (2006) ‘Using simulation to increase efficiency in blood supply chains’, Management Research News, 29(12), 801–819.

Sapountzis, C. (1984) ‘Allocating blood to hospitals from a central blood bank’, European Journal of Operational Research, 16(2), 157-162.

SAS (2017) ‘The ARMA Models’ retrieved from ‘SAS/ETS 14.3 User’s Guide’, SAS Institute Inc., Cary, NC, USA. 217-223.

SAS (2017) ’The ARIMA Procedure’ retrieved from ‘SAS/ETS 14.3 User’s Guide’, SAS Institute Inc., Cary, NC, USA. 218-328.

SAS (2017) ‘Forecasting Process Details’ retrieved from SAS/ETS 14.3 User’s Guide. *SAS Institute Inc., Cary, NC, USA*. 4150-4177.

Schmidt, P.J. (2002) ‘Blood and Disaster—Supply and Demand,’ New England Journal of Medicine, 346(8), 617.

Schreiber, G.B., Sharma, U.K., Wright, D.J., Glynn, S.A., Ownby, H.E., Tu, Y., Garratty, G., Piliavin, J., Zuck, T., Gilcher, R. (2005) ‘First year donation patterns predict long-term commitment for first-time donors’, VoxSanguinis 88 (2), 114–121.

Sha, Y. and Huang, J. (2012). The multi-period location-allocation problem of engineering emergency blood supply systems. Systems Engineering Procedia, 5, 21-28.

Shapiro, J.F. (2001) ‘Modeling the Supply Chain’ Duxbury Thomson Learning, Inc.

Simchi-Levi, D., Kaminsky, P. And Simchi-Levi, E. (2000), “Designing and Managing the Supply Chain”, Irwin McGraw-Hill

Sirelson, V., Brodheim, E. (1991) ‘A computer planning model for blood platelet production and distribution’, Computer methods and programs in biomedicine, 35(4), 279-291.

Solyal, O., Cordeau, J.F., and Laporte, G. (2015) ‘The Impact of Modeling on Robust Inventory Management Under Demand Uncertainty’, Management Science, 62(4), 1188-1201.

Soysal, M., Bloemhof-Ruwaard, J.M., Haijema, R., Vander Vorst, J.G. (2015) ‘Modeling an Inventory Routing Problem for perishable products with environmental considerations and demand uncertainty’, Int. J. Production Economics, 164, 118–133.

Srinivas, S., and Ravindran, A. R. (2017). Systematic Review of Opportunities to Improve Outpatient Appointment Systems. *In IIE Annual Conference. Proceedings* (pp. 1697-1702). Institute of Industrial and Systems Engineers (IISE).

Srinivas, S., and Rajendran, S. (2017) “A Data-Driven Approach for Multiobjective Loan Portfolio Optimization Using Machine-Learning Algorithms and Mathematical Programming” from *Chapter 8 in Big Data Analytics Using Multiple Criteria Decision-Making Models,* CRC Press; 175-210.

Stanger, S.H.W., Cotton, S., Wilding, R., and Yates, N. (2011) ‘Reduction of time expiry wastage in the blood supply chain by sharing stock’, Blood Stocks Management Scheme.

Stanger, S.H.W., Yates, N., Wilding, R., and Cotton, S. (2012) ‘Blood Inventory Management: Hospital Best Practice’, Transfusion medicine reviews, 2(62), 153-163.

Taha, H.A. (2017) Operations Research: An Introduction, Pearson; 10th edition

Taiwan Blood Services Foundation Statistics (2017) extracted from http://intra.blood.org.tw/upload/2dfb793b-06ce-4df7-affe-5acaecf6983a.pdf

Taiwan Blood Services Foundation. 2019 Annual Report. http://intra.blood.org.tw/upload/6657d89b-a4e0-4311-a704-ec2fd0a4ff61.pdf. Retrieved 23 February 2021.

Tarim, S.A., Manandhar, S. and Walsh, T. (2006) ‘Constraint Programming: A Scenario-Based Approach’, Springer, 11(1).

Tekin, E., Gurler, U., and Berk, E. (2001) ‘Age-Based vs. Stock level control policies for a perishable inventory system’, European Journal of Operational Research, 134, p. 309-329.

US General Accounting Office, (GAO) (2002) ‘Blood Supply Generally Adequate Despite New Donor Restrictions,’ GAO-02-754. Washington, D.C., As of October 10, 2016: http://www.gao.gov/assets/240/235235.html

Van Dijk, N., Haijema, R., van der Wal, J., Sibinga, C.S. (2009) ‘Blood platelet production: a novel approach for practical optimization’, Transfusion, 49(3), 411-420.

Vrat, P., Khan, A.B. (1976) ‘Simulation of a blood-inventory-bank system in a hospital’, Socio-Economic Planning Sciences, 10 (1), 7–15.

Wangboon, A., Phasukkit, P., and Keawbumrung, M. (2017) ‘Computational analysis of blood parameters separate by centrifuge technique’ Knowledge and Smart Technology (KST), 2017 9th International Conference on Chonburi, Thailand.

Wang, K.M., and Ma, Z.J. (2015) ‘Age-based policy for blood transshipment during blood Shortage’, Transportation Research Part E, 80, 166-183.

Weiss, H. J. (1980) ‘Optimal ordering policies for continuous review perishable inventory models’, Oper. Res. 28, 365–374.

Williamson, L.M., Devine, D.V. (2013) ‘Challenges in the management of the blood Supply’, Lancet381, 1866–1875.

World Health Organization. (2016) http://www.who.int/

Yates, N., Stanger, S., Wilding, R., and Cotton, S. (2017) ‘Approaches to assessing and minimizing blood wastage in the hospital and blood supply chain’, International Society of Blood Transfusion, ISBT Science Series, 12, 91–98.

Zaheer, H.A. and Waheed, U. (2016) ‘Blood transfusion service in disasters’, Transfusion and Apheresis Science, 55, 186–190.

Zhou, D., Leung, L.C., and Pierskalla, W.P. (2009), ‘Inventory Management of Platelets in Hospitals: Optimal Inventory Policy for Perishable Products with Regular and Optional Emergency Replenishments’, The 9th International Conference on Electronic Business, Macau.

Zhou, D., Leung, L.C., and Pierskalla, W.P. (2011), 'Inventory Management of Platelets in Hospitals: Optimal Inventory Policy for Perishable Products with Regular and Optional Expedited Replenishments', Manufacturing & Service Operations Management, 13(4), 420–438.

Vita

Han Shih

Han Shih is a doctoral candidate of Industrial Engineering and Operations Research in the Department of Industrial and Manufacturing Systems Engineering at the University of Missouri Columbia. He earned his M.S. in Industrial Engineering from the University of Missouri Columbia, M.S. in Management Science from National Chiao Tung University, Taipei, Taiwan, and B.S. Degree in Computer Science and Control Engineering from National Chiao Tung University, Taipei, Taiwan. He currently resides in Columbia, Missouri. Before he retired from Mizzou, he was a computing service manager at the University of Missouri. He is also a graduate teaching assistant at IMSE department. He is rewarded as Outstanding IMSE PhD Student for 2021. His research interests include supply chain healthcare systems, big data analytics, multiple criteria decision making, and supply chain optimization.