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Managing perishable inventories in healthcare services

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Abstract:

The management of perishable inventories is particularly challenging in healthcare field. One of the reasons lashing this is volatility, which is driven by irregular supply and stochastic demand. Exacerbated by a number of other factors such as the relatively short products shelf life, accelerated degradation and deterioration (premature expiration) and user specificity, such irregular supply and stochastic demand of perishable inventories bring additional challenges to the delivery of health services. This variability is likely to expose not only those in direct receipt of such healthcare products, but also the general population to insecure supplies. The norm in perishable products is to set an expiration date by which the product is best consumed. However, deterioration in products may accelerate, thereby; causing products to expire prematurely in random before their anticipated expiration date.

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With this in mind, the aim of the study is to explore how best to mitigate against inventory volatility in perishable inventory, which is characterized by random premature expiration, random demand, irregular supply, age differentiated demand and custom replenishment guidelines. Through the adoption of simulation-optimization along with new settings and replenishment policies, the optimized quantity level of daily orders could be determined for this combination of inventory restrictions. Owing to their custom medical compatibility guidelines, and their notable accelerated expiration, blood platelets were considered here. As study outcome, the emergent model presents a perspective of supply chains and their healthcare imperatives that will enable healthcare supply chain managers not only to discern, but also to interpret and facilitate the management and implementation of optimal inventories.

Keywords: Random Aging; Differentiated Demand; Perishable Inventory; Blood Platelets; Simulation; Optimization.

1. Introduction

Operations management literature alludes to considerable scholarly interest in understanding how the inventory of perishable products may be best enhanced for efficient matching of irregular supply to stochastic demand (Bakker et al., 2012; Janssen et al., 2016; Ali et al., 2017). Perishable products are characterized by their limited shelf life. By shelf life, we mean the period of storage wherein functional integrity is maintained and the product is deemed safe for use without any impediments.

In the literature of inventory management problems, a significant research only considers items that can be stored indefinitely (Moonsoo et al., 2019). Among such deal of research on perishable inventory, hardly one can find a work that addresses random shelf lives, instead, the major assumption is a fixed shelf life and deterministic expiration dates as in (Nahmias, 2011; Chapman et al., 2004; Stanger et al., 2012a, 2012b). However, gradual deterioration, contamination and obsolescence unavoidably shorten the products' shelf lives. This gradual loss in the functional integrity in the stored items makes their shelf life, not just shorter, but also stochastic. Deterioration results from different factors such as contamination, bacterial growth, damage, spoilage, dryness, vaporization, corrosion, ..., etc., which all contribute to shorter shelf-lives of perishable products

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such as foods, green vegetables, human blood, photographic film and many others (Zeinab et al., 2016).

The management of perishable inventory that is characterized by: *stochastic demand, stochastic supply, custom replenishment rules, age differentiated demand, and most importantly the stochastic shelf life*, all make the decision of when and how much to order more difficult to quantify (Moonsoo, et al., 2019). Among the different approaches employed to manage such a problem, simulation has been used to address some of the above border conditions in perishable inventory, (Janssen, Sauer, et al., 2018b). However, few studies can be found that employ simulation-based optimization that tackles the inventory problem of single or multi objectives (Mualla and Hasan, 2018; Gabriel et al., 2020; Hasan et al., 2020).

Simulation and optimization combined, can provide realistic solutions of NP-hard problems that cannot be analytically optimized. In the context of simulation-optimization, different applications could benefit from such a framework such as multi-echelon inventory systems under uncertainty (Yunfei et al., 2015), multi-objective optimization (Shing and Si, 2017; Sebastian et al., (2020), network structure (Wenhe Ye, Fengqi You 2016), transportation (Bierlaire, 2015), maintenance (Alrabghi and Tiwari, 2015) and decision making (Afsahi, et al., 2020).

One such perishable product attracting attention is human blood (Osorio et al., 2015; Janssen et al., 2016; Ageron et al., 2018). In this health related inventory, the inability to match blood supply to demand creates the potential for not only shortages but also overstocking and therefore waste (Van Dijk et al., 2009; Gunpinar and Centeno, 2015; Baş Güre et al., 2018). Thus, blood inventory management is not only a major healthcare management matter, but also one with a significant cost and financial footprint. In general, simulation-optimization was not sufficiently explored for the benefit of managing inventories of extremely perishable products that are characterized by: *stochastic demand, stochastic supply, custom replenishment rules, age differentiated demand, and stochastic shelf life* such as blood components.

What we know so far is that due to irregular supply and stochastic demand, the management of perishable inventories such as blood platelets is particularly challenging. We are also aware that

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there are serious patient-specific but also society-wide ramifications if the irregular supply and stochastic demand of blood platelets cannot be adequately managed. Taking these factors and other peculiar characteristics (assumptions) associated with blood platelet inventory management into consideration, the aim of the study is to explore how best to mitigate against inventory volatility, taking blood platelets as a typical case study for age differentiated demand. Using simulation-Optimization and SA, such exploration will be undertaken through the adoption of different settings and replenishment policies that allow for the determination of an optimized quantity level of daily-orders. Specifically, the following combined settings will be considered: stochastic demand, stochastic supply, custom replenishment rules, age differentiated demand, and most importantly the stochastic shelf life.

The remainder of the paper is organized as follows, a literature review is presented in section 2.0 followed by the decision conditions in section 3.0. The model is formulated in section 4.0 followed by a demonstration of the search algorithm in section 5.0. Next in section 6.0, an analysis of different scenarios is laid out to demonstrate the experimental part of the model followed by a sensitivity analysis in section 7.0. Finally, the paper concludes in Section 8.0.

2.0 The literature

There is a good deal of literature studies that cope with inventory systems of perishables products. These studies reveal the difficulty to determine the optimal parameters that provide a sound operation of the inventory while taking care of age categories of the on-hand quantities (Nahmias, 2011; Karaesmen et al., 2011). A number of scholars have sought to develop models to address the irregular supply and stochastic demand of perishable inventory to find such parameters. Among those, we would like to mention Prastacos (1984), Parlur (1985), Goyal and Giri (2001), Tekin, et al. (2001) and Bakker et al. (2012). Yet, in most settings of these studies, only deterministic shelf life is considered and the decision maker has a limited computational budget. The challenge thus is to establish a search procedure that consumes less computational time without the need for exhaustive search that may not be attainable for most of the cases. Accordingly, diverse approaches have been developed to deliver low-cost meta-models that seek to predict the profile of the objective function using the information attained from low number of point sampling, particularly for simulated scenarios. When the inventory problem advances by its border conditions, the

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analytical evaluation of the objective function may be unattainable. Such category can be stochastically simulated and simultaneously optimized to get the best solution via the so-called Simulation-Optimization.

Simulation-optimization refers to optimization via stochastic simulation (Chen & Lee, 2010). Simulation, which refers to the techniques and practices employed to imitate a specific behavior of a real system, is used to evaluate the objective function of an identified decision (solution vector). On the other hand, optimization is used to find the values of the solution vector that optimizes the objective function of interest. To search for the best solution vector, optimization techniques, regardless of their types, need to evaluate the objective function. Such an evaluation requires that the real system is operated (simulated) in every call of the optimization part. Since simulation can be demanding in terms of time and computational budget, the optimization should be guided to reduce the number of simulation calls. Simulation utilizes the knowledge, time, people to mimic systems, particularly when conducting real experiments is impractical or costly. Not only simulation can reduce the cost, it also accelerates the time without having to wait for a real operation of a system. By implementing Simulation-Optimization to develop an approach that efficiently searches the solution space, the search approach has to be custom-built to reduce the computational expenses while providing quality solutions. However, as stated by Wilson et al., (2020), problems of higher sizes of solution vectors result in a vast search space, thereby, exceeding the computational power and time available to complete all the possible solutions. This category of problems is considered as NP-hard (He et al., 2017; Herrmann, 2013).

According to Banks (1998), Chen et al. (2013), and Xu, Huang, Chen and Lee (2015), a simulation optimization problem is established by optimizing an expected value of some objective function. Simulation optimization has been considered in different research studies and applications. In the field of transportation for instance, Bierlaire (2015) presented a review of simulation optimization to in transportation. In maintenance, Alrabghi and Tiwari (2015) addressed the simulation optimization applied to maintenance systems. Similar simulation optimization research can be found on the problem of balancing assembly lines (Dagkakis et al., 2019). Patient schedule using simulation optimization can ber found in similar research of Rezaeiahari and Khasawneh (2020). Other applications that benefit from simulation optimization approaches include sustainably in

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ground water operations (Park et al., 2020). Not only the production field, simulation optimization has been also applied in the service sector, for instance, a stochastic simulation-optimization model for base-warranty and extended-warranty decision-making has been developed. Moreover, to solve different problems in renewable energy such as building thermal load management through integration of solar systems, simulation optimization was the approach of choice (Habib et al., 2020).

A recent review by Juan et al. (2015) talks about metaheuristics applied in simulation optimization and stochastic combinatorial problems. Another review can be found in the work of Kleijnen (2017) which addresses Kriging metamodeling in simulation. As for optimization, a review about different categories of search algorithms can be found in research of Xu et al. (2015). Their work addressed sample-path, gradient-based methods, stochastic constraints and multi-objective optimization. Unlike exhaustive search methods, metaheuristics are generic forms of the solution search process without guarantees of global optimality, however, with reduced computational time (Sörensen, 2015).

By considering platelets as typical items that are characterized by rapid ageing, compatibility, stochastic demand and premature expiration, a reliable optimization approach is required to solve this stochastic problem. Interested readers can find useful reviews on hybrid metaheuristics in (Lozano and Martinez, 2010; Blum et al., 2011). Among those metaheuristics is Simulated Annealing (SA) which has been found effective in many industrial and services applications (Munku et al., 2020; Novita et al., 2019). The interesting feature in Simulated Annealing is its ability to jump out of local minima and the ability to handle objective functions of coarse profiles. SA will be tailored to fit the proposed inventory policy of this study.

Considerable research efforts have been undertaken for perishable inventory management in the context of health, food and drug industry. For example, Parlar (1985) developed a model that categorized perishable inventory into two age categories with proportions of one category satisfying the other. In Duan and Liao (2013), a model was proposed to maintain old inventory ratios (OIR) for perishable inventory (blood platelets) that minimized system outdates' costs. The

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literature also discusses novel allocation strategies for blood inventories that are able to explore the tradeoffs between age and transfused blood availability (see Atkinson et al., 2012).

2.1 Models focused on blood platelets as perishables

At this point, it is perhaps pertinent to explore what we mean by *accelerated* degradation and deterioration. *Accelerated* degradation and deterioration is a condition that can lead to early, in effect, premature expiration and spoliation (Bosman et al., 2008; Zubair, 2010; Williamson and Devine, 2013; Salins, 2015; Wong et al., 2016).

There are about four major components of blood that are entitled to be perishable – *platelets*, red and white blood cells and plasma. With the exception of plasma, blood components are generally perishable and have a relatively short shelf life (Nahmias, 2011; Chapman et al., 2004; Stanger et al., 2012a, 2012b; Kopach et al., 2008; Hess 2010; García-Roa et al., 2017).

Platelets (also known as *thrombocytes*) are a key blood component responsible for the clotting (*coagulation*) of blood following injury and bleeding (Machlus et al., 2014). Although only around 10% of total blood transfusions is platelet-specific, its availability and use is essential in healthcare. For example, cancer (leukemia) patients suffering bleeding complications often require platelet transfusions in order to prevent bleeding from ruptured blood vessels (Izak and Bussel, 2014). Platelets transfusion is also required to prevent bleeding for a range of other patients – for example, those undergoing organ transplants (Stroncek and Rebullá, 2007). These factors all mean that platelets remain an invaluable healthcare product.

In addition to the existing models on perishable products, there are existing models that specifically focus on *blood platelets as perishables* (Haijema et al., 2007, Van Dijk et al., 2009; Haijema, 2011; Zhou et al., 2011; Dalalah et al., 2018; Rajendran and Ravindran, 2019). For example, Haijema et al. (2007) explored the production of blood platelets utilizing dynamic programming that focused on age differences of platelets. In their more recent study, again utilizing dynamic programming, Haijema et al. (2009) developed a practical ‘*order-up-to*’ inventory rule for optimal blood platelet production. The rule requires an organization to regularly review its inventory position. Following such review, ‘*orders*’ are then issued to ensure that inventories are surfaced ‘*up-to*’ a specifically

defined level (Chen and Disney, 2007). Zhou et al. (2011) appraised the dynamics of platelet inventory management finding that optimal costs were particularly impacted by uncertainty in a number of areas including demand uncertainty and the age of orders that were expedited. Duan and Liao (2013) study focused on the age factor and found that centralizing the supply chain greatly reduces platelet outdate rates by about 18.56%. In both Gunpinar and Centeno (2015) and Rajendran and Ravindran (2019), stochastic integer programming models were developed to reduce platelet scarcity and waste levels. In Dalalah et al. (2018), taking into consideration age-differentiated and stochastic demand, a model able to optimize stocking decision variables by minimizing the overall inventory costs was developed. Overall, it is observed that the models which emerge from these reviewed studies do not appear to have explicitly taken into consideration accelerated degradation and deterioration of platelets. However, the literature suggests that this phenomenon is part and parcel of perishable items such as blood platelets (Bosman et al., 2008). Our premise is that accelerated degradation and deterioration will lead to premature expiration of blood platelets kept in storage. This will ultimately create a condition where platelets are characterized by among other decision conditions, '*Random inventory expiration lifetimes*'. Thus, the main difference between Dalalah et al. (2018) and this present study is that in Dalalah et al. (2018), three inventory management decision conditions were considered. These decision conditions are (i) '*Age-differentiated demand*' (ii) '*Stochastic demand*' and (iii) '*Specific inventory issuance policy*'. In the present study, five decision conditions will be considered (i) '*Age-differentiated demand*' (ii) '*Customized replenishment decisions*' (iii) '*Custom inventory and order fulfillment policy*' (iv) '*Different costs considerations*' and most importantly (v) '*Stochastic inventory expiration lifetimes*'.

Blood components have relatively short shelf lives (Fontaine et al., 2009; Chandra et al., 2014; Civelek et al., 2015; Rajendran and Ravindran, 2019). To put this into perspective, with advances in technology, the shelf life of blood plasma is about 365 days (Prastacos, 1984; Schneider, 1995; Arya et al., 2011). Conversely, that of red blood cells is approximately 42 days (Cancelas et al., 2015; García-Roa et al., 2017). However, on average, the shelf life of platelets is approximately between 3 and 5 days or seven days at the very most (Chandra et al., 2014).

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Premature expiration which results in shorter shelf life of platelets means that anything between 4% (Hess et al., 2000), 17% (AABB, 2011) and 20% (Haijema et al., 2007; Verma and Agarwal, 2009) of collected platelets samples is outdated. Inevitably, this implies that a substantial amount of blood platelets are wasted due to expiration while in storage (Van Dijk et al., 2009).

The demand for platelets in addition to its relatively limited shelf *life* is further complicated by its usage which is age-differentiated (Kok and Fisher, 2007; Acimovic and Graves, 2012). Indeed, the treatment of some medical conditions requires platelets of specific, but different ages. For instance, treatment of hematology and oncology conditions generally require new platelets (Haijema et al., 2007; Van Dijk et al., 2009; Civelek et al., 2015).

What we realized so far, is that the management of perishable inventories such as blood platelets is especially difficult due to intermittent supply and stochastic demand. We are all mindful that if the erratic supply and stochastic demand, premature expiration and differentiated demand of blood platelets can not be properly controlled, significant patient-related but even social consequences may be encountered. Taking these variables and other problem specific features associated with inventory control of blood platelets into consideration, this study comes with a purpose to examine how best to protect against inventory variability of blood platelets. Such research would be conducted by implementing various settings and replenishment policies using simulated annealing for optimization and discrete event systems for simulation that allow finding an optimum order quantity which minimizes the overall cost and demonstrates a smooth operation of the inventory.

3.0 The decision conditions

In order to achieve the study aim, a hybrid analytical perspective developed through a model that encompasses five decision conditions are now discussed. These decision conditions are (i) '*Age-differentiated demand*' (ii) '*Customized replenishment decisions*' (iii) '*Custom inventory and order fulfillment policy*' (iv) '*Different costs considerations*' and most importantly (v) '*Stochastic inventory expiration lifetimes*'.

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3.1 Random aging and age-differentiated demand

When a platelet is in storage, it ages over time. Aging can be *deterministic*, resulting in a specific expiration date. It can also be *stochastic* resulting in what could be deemed as unanticipated premature expiration. While there is ample literature on perishable products of fixed shelf lives (Goyal and Giri, 2001; Kouki and Jouini, 2015; Gaukler et al., 2017; Firoozi and Ariaifar, 2017), there is less literature available on randomized *accelerated* deterioration of perishable products.

A blood platelet arguably can lose its functional integrity *any time earlier* than its expected expiration date (Bosman et al., 2008). This can be shown as follows. Assume that a platelet has a shelf life of ' A ' and denote the corresponding ages of a platelet by $i = 1, \dots, A$ in days, where ' A ' is an integer number. Hence, platelets that are able to maintain their functional integrity beyond ' A ' are deemed not to have expired. However, as expiration is stochastic, some platelets may expire prematurely before reaching A -days old. Spoilage will therefore result from premature expiration due to accelerated platelet degradation and deterioration.

The proposed approach can handle any shelf life of $A > 0$ at the expense of computational time. Here, we consider a shelf life duration of $A=5$ days, which fits the literature position on the lifetime of blood platelets in hospital storage (see Chandra et al., 2014). In effect, a platelet with a shelf life of five days ($A=5$ days) will go through five different ages each of its own daily demand. To better simplify this notation, the five ages may be referred to as '*Fresh*' (...of 1 day old), '*Young*' (...of 2 days old), '*Mature*' (...of 3 days old), '*Old*' (...of 4 days old) and '*Elderly*' (...of 5 days old). Platelets deemed '*Elderly*' (...of 5 days old) will exceed their shelf life if not used on the fifth day of storage. It is however important to note that '*Elderly*' platelets are not the only platelets prone to spoilage. This is because, all platelets irrespective of age, may stochastically expire due to accelerated degradation and deterioration.

3.2 Customized replenishment decisions

Stock replacement need to be considered prior to expiration, therefore, the replenishment decisions within perishable inventory management are influential. Examples of replenishment decisions include '*random issuing*', '*youngest items first*' and '*oldest items to leave first*'. We sought to apply an easy-to-implement fixed-order quantity policy in the proposed study (see Kostic, 2009).

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Thus, only newer ‘*Fresh*’ platelets are replenished. No replenishment is carried out for other ages, as excess ‘*Fresh*’ platelets will age daily while in storage. Thus, sufficient quantities of ‘*Fresh*’ platelets will eventually meet demands for older platelets. The daily-order quantity of ‘*Fresh*’ platelets is the decision variable that has to be found for a planning period of $T=365$ days. We assume that the delivery time (lead-time) of ordered quantities does not consume from platelet lifetime, thereby; ‘*Fresh*’ platelets are only one day old.

When an exact age match is not found, patients who need newer platelets will have higher priority to receive substitutes. When platelets of a certain age, for example, ‘*Mature*’ are required, and the exact age specification is not available, the demand will be *first* satisfied by supplying the patient with platelets of the next age. In this scenario, the patient is first provided with ‘*Old*’ and then ‘*Elderly*’ platelets. Conversely, if these older aged platelets are not available, then demand by a patient requiring ‘*Mature*’ platelets will be satisfied by providing the patient first with ‘*Young*’ and then ‘*Fresh*’ Platelets. These replenishment decisions are illustrated in Table 1 (below). The table demonstrates a preference matrix for an utmost shelf life of ‘*A*’ (1 being most desirable).

Table 1: Age preference for a maximum shelf life of “*A*” days

		Demand by:						
		Age						
		1	2	3	...	A-2	A-1	A
Supply from:	age							
	1	1	A	A	...	A	A	A
	2	2	1	A-1	...	A-1	A-1	A-1
	3	3	2	1		A-2	A-2	A-2
	⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮
	A-2	A-2	A-3	A-4		1	3	3
	A-1	A-1	A-2	A-3	...	2	1	2
	A	A	A-1	A-2	...	3	2	1

*1 is most preferred, A is least preferred.

A special case of Table 1 results for platelets of a shelf life of 5 days. In Table 5, we show the preferences in compatibility when $A=5$. In this study, there is no protection provided against any demand for older platelets. In effect, a core assumption in this study is that newer platelets can be utilized without any limit to satisfy any demand for older platelets.

Table 2: Compatibility preference of the five ages

		Demand by:				
		Age				
		<i>Fresh</i>	<i>Young</i>	<i>Mature</i>	<i>Old</i>	<i>Elderly</i>
age	1	2	3	4	5	
Supply from:	1	1	5	5	5	5
	2	2	1	4	4	4
	3	3	2	1	3	3
	4	4	3	2	1	2
	5	5	4	3	2	1

3.3 Random inventory lifetimes

The proposed model takes two expiration factors into consideration. The *first* which is deterministic, assumes that the shelf life duration will be exceeded before any need for the platelets materializes (we refer to this as outdates). The *second* consideration assumes that not only can platelets experience accelerated degradation and deterioration (leading to premature expiration), but that due to the compounded nature of sample testing, treatment, manipulation and storage, *different* platelets will experience *different* acceleration rates of degradation and deterioration. Thus, the shelf life of platelets in this case can be modelled by different distributions. These activities can be shown utilizing a differential equation where quantity is N and the exponential decay constant (a positive rate) is λ :

$$\frac{dN}{dt} = -\lambda N . \quad (1)$$

The solution of the above is simply given by

$$N(t) = N_0 e^{-\lambda t} , \quad (2)$$

where N_0 is the initial inventory quantity. The percent of surviving quantities of platelets (that is, non-expired) by time t is shown as $\frac{N(t)}{N_0} = e^{-\lambda t}$, which resembles the exponential reliability function $R(t) = e^{-\lambda t}$. Note that, $R(t) = 1 - F(t)$, where $F(t)$ is the cumulative distribution of the lifetime. Therefore, the resulting lifetime distribution of such a reliability function is given by

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$$f(t) = \lambda e^{-\lambda t}, \quad t > 0 \quad (3)$$

and the mean lifetime is $\frac{1}{\lambda}$. The hazard function $z(t)$ of exponentially distributed lifetime is constant; that is:

$$z(t) = \frac{f(t)}{1-F(t)} = \frac{\lambda e^{-\lambda t}}{e^{-\lambda t}} = \lambda. \quad (5)$$

Considering degradation and deterioration, at the beginning of each day, we can compute the probability of a platelet maintaining its functional integrity given its current age by a conditional probability. The exponential conditional reliability gives the probability for platelet survival of t duration, having successfully accumulated T unit time of survival. The exponential conditional reliability function is

$$R(t|T) = \frac{R(T+t)}{R(T)} = \frac{e^{-\lambda(T+t)}}{e^{-\lambda T}} = e^{-\lambda t} \quad . \quad (6)$$

The above suggests that the reliability function of exponential platelets deterioration is the same regardless of the time that the platelet has experienced while in storage. To simulate this aging process, the probability of a platelet maintaining its functional integrity for the next t days – given it has survived up to T – is given by $e^{-\lambda t}$. Therefore, we apply a stochastic model to probabilistically eliminate those platelets which may not be able to maintain their functional integrity. That is, each platelet will maintain functional integrity up to t with a probability of $e^{-\lambda t}$, and will prematurely experience degradation and deterioration with a probability of $1 - e^{-\lambda t}$, where $t = 1$ if tested every day. For instance, suppose that five platelet units exhibiting a deterioration rate of 0.3 are currently available in the inventory (labelled 1 to 5). The conditional probability of maintaining functional integrity by one more day is given by $e^{-0.3*1} = 0.74$. Suppose the following random number stream (i.e. uniform $[0, 1]$) = 0.5, 0.8, 0.3, 0.9, 0.1) is considered as an instance to simulate platelets being able to maintain their functional integrity beyond their expiration date. Thus, platelet units 1, 3 and 5 will maintain their functional integrity to the next day. However, platelet units 2 and 4 will prematurely expire. This procedure is simulated for every platelet unit of every age in the inventory. Of note; other random number

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streams give other results; hence, Monte Carlo simulation is an essential tool for modelling lifetimes. This contends that platelet expiration discussed in the literature review will result in the need to consider premature expiration at a deterioration rate of 20%, which will result in $\lambda=0.045$ and a corresponding lifetime distribution of $f(t) = 0.045e^{-0.045t}$ in days, where $F(5)=0.2$.

3.4 Inventory status and issuance policy

The demand probability distribution of platelets is likely to differ by age. For example, it is plausible for the demand of ‘*Fresh*’ platelet types to follow a Poisson distribution. On the other hand, demand for ‘*Young*’ platelet types may follow a normal distribution. The proposed model will take into consideration two inventory policies: the *first*, is where order fulfillment has only exact age match (in other words, ‘*No-Compatibility*’), and the *second* is where order fulfillment allows for age mismatch (‘*With-Compatibility*’).

On the start of each typical day, an inventory count is undertaken to record the age of all platelets’ units. Medical research suggests that, traditionally, platelet incompatibility was not construed to hinder use and, in fact, transfusion using age mismatched platelets has been common practice (see Djerassi et al., 1963). However, more recently, it will appear that medical science has begun to consider that incompatibility brings adverse consequences for platelet recipients (Valsami et al., 2015). Thus, on the basis that platelet substitution by compatibility is *untenable*, the available quantities of platelets per age will be counted at the beginning of each day, and then the demand will be satisfied by supplying users with platelets that meet their precise age requirements. If there is a shortage of a platelet of a specific age, that shortage is recorded. Hypothetically, if platelet substitution by compatibility is *tenable*, available supplies within the inventory are counted and demand is fulfilled by supplying users with an exact match first. If shortages in exact matches occur, a search is undertaken to find a compatible substitute from the remaining platelets held in storage. Substitution is achieved based on the preferences shown earlier in Table 1. On satisfaction of demand, shortages (if any) are recorded, prematurely expired platelets are then removed, and inventory of ‘*Fresh*’ platelets is replenished.

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3.5 Different costs consideration

Pricing and costs is a major decisional condition that must be integrated into perishable inventory management decisions (Chen et al., 2014). Generally, pricing and costs in inventory may be of two types. The first is where prices and costs do not change over a period of time even when product demand (and/supply) changes over that same time period. The second type will generally allow for price and costs changes as a demand (and/supply) or inventory function over time. The second scenario is what organizations dealing with products that must be utilized with a specific fixed period of time (perishable products) usually experience. In this study, the cost components have been roughly estimated based on projected cost estimates of producing and storing platelets. For platelets of all ages, shortages costs are estimated to be US\$500 while costs of outdated and premature expiration are US\$200. The mismatch cost is US\$20 (regardless of platelet age), while the holding cost is set to US\$1/unit/day.

4.0 Formulation

When platelets survive only one day (i.e. $A=1$), the proposed model is reduced to a classical newsvendor problem. In contrast, when the lifetime is greater than one day (i.e. $A>1$), this means that each platelet will have a wider window in terms of time to be used/consumed. For consistency with periodic inventory counting, daily updates to the model is undertaken. Consequently, for a year - long planning period, 365 demand vectors are realized.

The following nomenclature are employed for model notations:

t : The planning period of a day T , $t = 1, \dots, T$.

i : Platelet age, where $i = 1, \dots, A$.

D^t : The demand vector of all ages in day t , where, $D^t = [d_1^t, d_2^t, \dots, d_A^t]$.

S_i^t : Platelet resulting shortage of age i , end of day t .

O_i^t : Outdated platelets of age i , at day t end (only age A will outdate anyway).

P_i^t : Prematurely expired quantity of age i end of day t .

x_i^t : Platelets of age i beginning of day t that are available.

X^t : The inventory status of platelets differentiated by “ A ” lifetime periods start of day t where,

$$X^t = [x_1^t \quad \dots \quad x_A^t]^T.$$

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BL_i^t : Accumulation of platelets of specific age i which is not satisfied by exact age match in day t .

IC_i^t : “Platelets Consumed” is the amount of the platelets of age i that have been used to satisfy demand of platelets of other ages, end of period t .

IS_i^t : “Platelets supplied” is the quantity of platelets of another age that is supplied in order to meet demand of platelet age i on day t .

Q : The decision variable (order quantity). In our model, the only platelets that are restocked are one-day-old platelets.

The transition in the state of the inventory evolves daily according to the earlier identified decision conditions; that is (i) ‘Age-differentiated demand’ (ii) ‘Customized replenishment decisions’ (iii) ‘Custom inventory and order fulfillment policy’ (iv) ‘Different costs considerations’ and most importantly (v) ‘Stochastic inventory expiration lifetimes’. Given the current inventory state (the specific quantity of platelets available for use at the start of each day), a new inventory status is met by first meeting realized platelet demand by exact age match following which compatible substitutes are pursued. This daily accumulation of platelets by age i after being met (satisfied) by exact match, can be expressed as

$$BL_i^t = [d_i^t - x_i^t]^+, \quad \forall i = 1, \dots, A, \quad (7)$$

Where $[z]^+$ is the $\max(z, 0)$. If $BL_i^t > 0$, a substitute will meet BL of all ages, or up to the point that the on-hand inventory of platelets of compatible ages are used. The total quantity employed in meeting demand for platelets of age i by substitution (flowing only from compatibility) is denoted by IS_i^t . Thus, platelets shortage observed for age i at the end of day t is given by

$$S_i^t = [BL_i^t - IS_i^t]^+, \quad \forall i = 1, \dots, A. \quad (8)$$

Equation (8) must be undertaken on an age-by-age basis commencing with age 1. IS_i^t is also updated in line with age based platelet use. Having said that, the state of inventory (which is represented as x_i^t) is updateable using quantities and ages. Generally, for every t ,

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$$\text{Quantity update: } \tilde{x}_i^t = [[x_i^t - d_i^t]^+ - IC_i^t]^+ - P_i^t \quad i = 1, 2, \dots, A \quad (9)$$

$$\text{Age update: } x_i^{t+1} = \begin{cases} Q & i = 1 \\ \tilde{x}_{i-1}^t & i = 2, \dots, A \end{cases} \quad (10)$$

Outdates end of t can also be shown as

$$O_A^t = x_A' . \quad (11)$$

Equation (9) above indicates that a specific aged platelet is used based on it being either (i) a precise match, (ii) a substitute based on its compatibility, or (iii) following premature expiration. The outdated quantity of platelets at the end of day t is represented by the outstanding platelet units of age A shown by O_A^t . The prematurely expired quantity P_i^t is found following the procedure presented earlier in *equations* (1) - (6).

In equation (10), all platelets become older by one day as their residual shelf life reduces and ‘*Fresh*’ platelets are replenished and taken into storage. Inevitably, the next day ($t+1$), the available inventory becomes the commencing inventory. The replenished quantity of platelets Q will be available the next day. Note that, in the proposed model, an ‘*order-up-to-level*’ policy (see Chen and Disney 2007) will be construed in the same manner as a ‘*fixed-order*’ policy since the inventory “*age I*” will always be empty at the time of replenishment.

Shortages of platelets of age i are shown as S_i^t . Conversely, *system shortages* over a period of planning T can be represented as $\sum_{t=1}^T S_i^t$; based on these, the entire *system shortage* of platelets of age i becomes

$$SS_i = \sum_{t=1}^T S_i^t, \quad i = 1, \dots, A. \quad (12)$$

Premature expiration is experienced at the end of each day. The total premature expiration of platelets of each age is

$$SP_i = \sum_{t=1}^T P_i^t, \quad i = 1, \dots, A. \quad (13)$$

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Similarly, platelets reaching their expiration due to aging are only to those of age “ A ” where, $SO_1 = SO_2 = \dots = SO_{A-1} = 0$; That is,

$$SO_A = \sum_{t=1}^T O_A^t . \quad (14)$$

The cost of shortages of platelets of age i is represented as sc_i and cost associated with outdateding due to aging (which is the same as premature expiration cost) is denoted by oc_i . Denoted by h is the cost associated with holding platelets in inventory for one day. The holding cost is the multiplication of h times the average inventory, where the average inventory of platelets of age i over T is approximated by $\bar{x}_i = \frac{\sum_{t=1}^T x_i^t}{T}$. The average age of the inventory is also estimated by $\bar{A} = \frac{\sum_{t=1}^T \sum_{i=1}^A ix_i^t}{\sum_{t=1}^T \sum_{i=1}^A x_i^t}$. A substitution matrix can be established which exemplifies the amount of platelets of a specific age which are utilized to meet a specific demand. The matrix is shown as

$$M^t = \begin{matrix} & \begin{matrix} \text{age 1} & \text{age 2} & \dots & \text{age A} \end{matrix} \\ \begin{matrix} m_{11}^t & m_{12}^t & \dots & m_{1A}^t \\ m_{21}^t & m_{22}^t & \dots & m_{2A}^t \\ \vdots & \vdots & \ddots & \vdots \\ m_{A1}^t & \dots & & m_{AA}^t \end{matrix} \end{matrix} \quad (15)$$

The matrix above suggests that platelets aged 1 are fulfilled by a quantity of precise match m_{11}^t , plus some aged 2 (m_{12}^t) and so on. At the same time, age “ A ” platelets are fulfilled by $\sum_{i=1}^A m_{Ai}^t$. For the entire planning period, the total substitution matrix $\mathbf{M} = \sum_{t=1}^T M^t$, which results in

$$\mathbf{M} = \begin{bmatrix} M_{11} & \dots & M_{1A} \\ \vdots & \ddots & \vdots \\ M_{A1} & \dots & M_{AA} \end{bmatrix} . \quad (16)$$

The matrix \mathbf{M} constitutes of the aggregate distribution of the amounts used for exact and compatible substitution. The quantity fulfilled by newer platelets is a summation of lower triangular elements, $L = \sum_{i=1}^A \sum_{j=1}^A M_{ij} , \forall i > j$, conversely, demand fulfilled by platelets that are older (upper triangular elements) are determined by $U = \sum_{i=1}^A \sum_{j=1}^A M_{ij} , \forall i < j$. Demand fulfilled

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by precise matches is designated the diagonal sum and represented as $\sum_{i=1}^A M_{ii}$. Mismatch (substitution) cost is shown as $mc_{a>b}$ for fulfilling age a platelets by those of age b , where $a > b$ (i.e. cost of substitution by newer platelets). Similarly, the cost of substitution by older platelets is $mc_{a<b}$, where $a < b$. Recall the system shortage SS_i , the premature expiration SP_i , and outdates SO_A from equations (12-14), it becomes possible to represent the cost objective function as a combination of six components, *first*, the holding cost $\sum_{i=1}^A h \times \bar{x}_i$, *second*, the shortage cost $\sum_{i=1}^A (sc_i \times SS_i)$, *third*, the premature expiration cost $\sum_{i=1}^A SP_i \times oc_i$, *fourth*, outdates cost $SO_A \times oc_A$, *fifth*, mismatch cost due to order fulfillment with younger platelets $L \times mc_{a>b}$, and finally the cost due to order fulfillment with older platelets $U \times mc_{a<b}$, that is:

$$\min \sum_{i=1}^A h \times \bar{x}_i + \sum_{i=1}^A (sc_i \times SS_i) + \sum_{i=1}^A SP_i \times oc_i + SO_A \times oc_A + L \times mc_{a>b} + U \times mc_{a<b} \quad (17)$$

Table 3: Inventory of five days' shelf life over a three day planning period

Initial inventory of all ages: (5,2,3,7,0)	Day 1 Demand: (2,3,3,1,0)	Day 2 Demand: (3,1,0,0,0)	Day 3 Demand: (1,1,4,0,1)
Inventory after exact match	3,0,0,6,0	2,1,0,0,3	3,0,0,0,0
Backlog upon exact age match	0,1,0,0,0	0,0,0,0,0	0,0,4,0,1
Inventory after age mismatch	3,0,0,5,0	2,1,0,0,3	0,0,0,0,0
Shortage end of day t	0,0,0,0,0	0,0,0,0,0	0,0,1,0,1
Premature expiration*	1,0,0,2,0	1,1,0,0,1	0,0,0,0,0
Remaining inventory after premature expiration	2,0,0,3,0	1,0,0,0,2	0,0,0,0,0
Outdates end of period t	-, -, -, -, 0	-, -, -, -, 2	-, -, -, -, 0
Replenishment quantity*	5	4	6
Inventory ready for next day	5,2,0,0,3	4,1,0,0,0	6,0,0,0,0

	Totals	Day 1	Day 2	Day 3
Shortage	2	0	0	2
Premature Expiration	6	3	3	0
Outdates	2	0	2	0
Average inventory*	7.000			
Average age of inventory*	1.714			
Shortage cost (\$)/day	$2 \times 500 / 3 = 333.33$			
Premature exp. and outdate costs (\$)/day	$8 \times 200 / 3 = 533.33$			
Holding cost (\$)/day	7.00			
Age mismatch cost (\$)/day	$4 \times 20 / 3 = 26.67$			

*Premature expiration should be simulated. For the purpose of demonstration, the quantities provided in this example are by assumption.

*Replenishment quantities by assumption.

*Based on inventory ready for next days.

“-” means inapplicable quantity.

Table 3 (below) is an illustrative inventory status example for platelets of five days' shelf life over a three-day planning period. Note that, premature expiration can only be attained via simulation following the procedure explained earlier in *equations* (1)-(6) while the replenishment quantities can only be attained by optimization. However, for demonstration purposes, both quantities (those are, premature expiration and replenishment quantities) are determined by assumption.

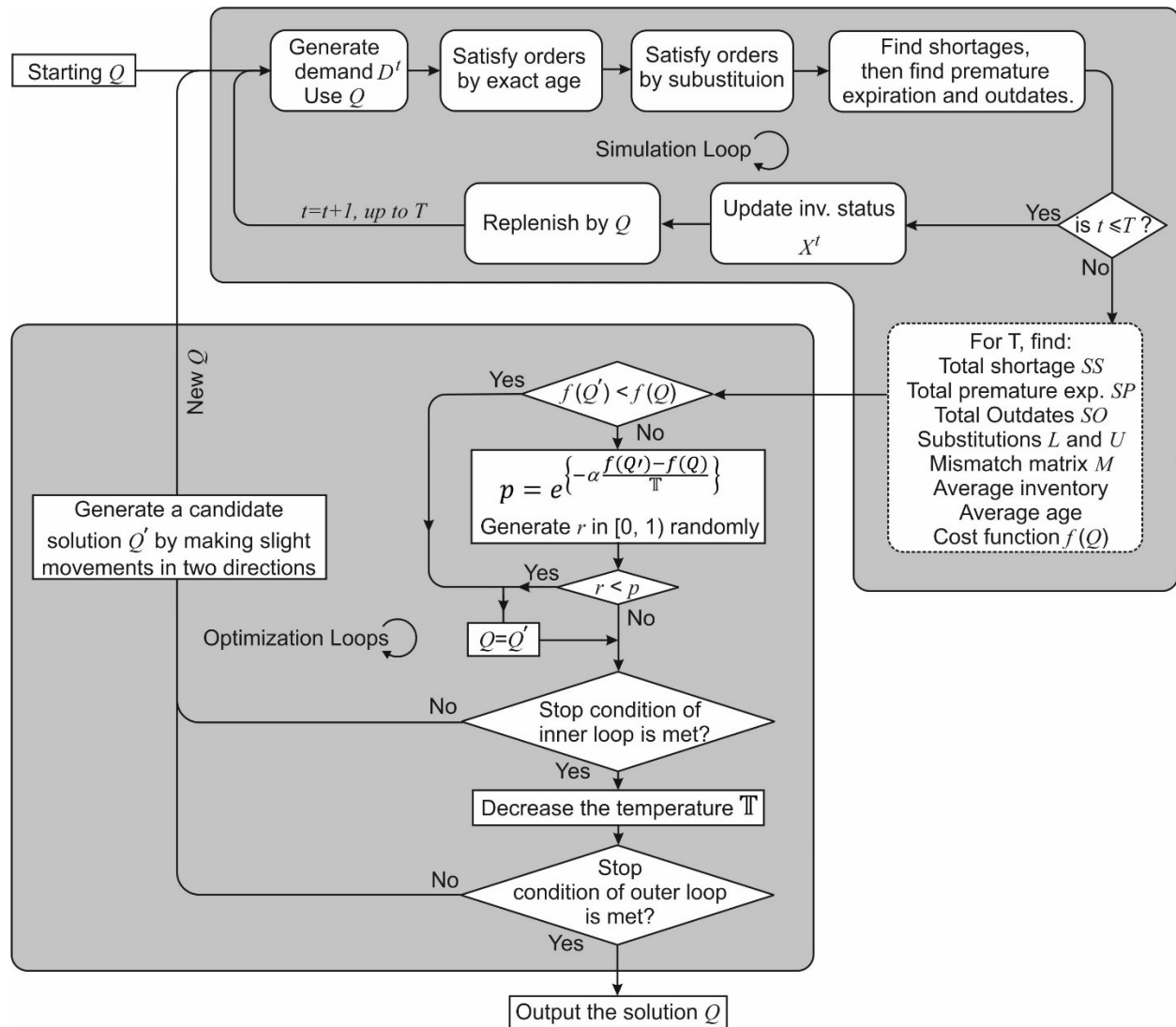
5.0 The search algorithm

Random demand streams will be generated via simulation in the proposed model. Similarly, to establish premature expiration, data of predetermined mean lifetimes will also be simulated. The inventory evolution over time will also be simulated in order to find (i) shortage, (ii) premature expiration, and (iii) outdates. For these reasons, evaluation of the objective function articulated in equation (17) is only really plausible by simulation for every Q over a certain planning period T . Different replenishment quantities of platelets result in different objective functions; hence, we propose a custom designed search algorithm to guide the search for optimality.

Since platelets demand is random, which in turn affects the resulting daily on-hand inventory, the objective function becomes stochastic with possible local minima. However, because it is relatively smooth in its profile, search algorithm such as Simulated Annealing (SA) will be efficient in climbing local optima. Simulated Annealing (SA) is a probabilistic optimization approach (Kirkpatrick et al., 1983). The superiority of SA over other approaches is that SA is able to cater for cost functional arbitrariness associated with different profiles.

For every trial of SA , platelets inventory is simulated for T cycles as shown in the top right loop of Figure 1 (which is a diagrammatical representation of our simulation and optimization collaboration).

Figure 1: Schematic diagram of simulation-optimization frameworks



It must be noted that there is a complementary mutual concatenation between simulation and optimization. Each simulation run implements the decision vector (Q) to evaluate the objective function. The decision vector is determined following a search undertaken through optimization. What this means is that the search for the next move is guided by the output of simulation (emanating from the optimization algorithm). The output is transferred to the key SA optimization loop and the cycle repeats. There is a requirement for simulation to trigger daily random demands as well as for the operation of stochastic SA while MATLAB is employed to build a code library for the simulation and the search algorithm. The built code library can adapt to any platelet age settings. For this reason, it is possible to differentiate platelet demand by as many iterations of age

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as may be required. All stochastic parts in the model including premature expiration, random demand and stochastic search are dependent on random number generation such as Monte Carlo simulation.

Commencing with an initial solution Q , a simulation of platelet inventory is undertaken over the entire duration of planning. Next, a new solution neighborhood is found which can be located by considering the degree of shortages and outdates. Shortages guide the search to increase the quantity of platelet orders, while observed outdates guide the search to lower platelet quantities. If both shortages and outdates are observed (which is the most common scenario while searching), the higher quantity will have more influence on the search direction.

A neighborhood is identified by moving a step Δs in some direction. During the search undertaken within the different neighborhoods, there is a variation with the step size that is dependent on a schedule. The step size is reset to its original value at any point in time that the algorithm proceeds to a new neighborhood. Simulation is utilized to test the value for objective function at every point in time moves are made. At any point an improved value emerges, the solution is accepted, otherwise, rejected with a probability given by $e^{\{-\alpha \frac{f_{new}-f_{old}}{\mathbb{T}}\}}$, where the following nomenclatures are employed for notations:

\mathbb{T} : Temperature

f : Value of cost function value (for both existing and new solutions – in effect, the decision variable).

$\alpha > 0$: Tuning parameter.

As experienced in any conventional simulated annealing, there will be a cooling of temperatures while the search is being undertaken due to a multiplicative factor θ , where $0 < \theta < 1$. The algorithm will generally cease to run at the point that no compelling enhancements to the objective function is ascertained or alternatively when the maximal number of search trials have been run. The solutions that are deemed viable will be those seen to fulfill non-negative upper and lower limits.

6.0 Analysis

6.1 The scenarios

For performance tests of the model that is proposed, a two-phased analysis is employed. *First*, the robustness of the search algorithm is tested by comparing the results with analytically solved models – in this case, the classical newsvendor. *Second*, analysis is undertaken based on testing the five conditions against four different *inventory status and issuance policy* scenarios. In all experiments below, the following search parameters were used: $\alpha = 0.9$, $\theta = 0.5$ and a starting temperature (T) of “1” which cools down as the algorithm advances in the search process.

6.2. Analysis 1 (Comparison with the classical newsvendor)

By considering platelets of a one-day shelf life, the proposed model will be reduced to the classical newsvendor problem in that platelets will need to be disposed if not used the same day. Considering normal distribution $N(\mu, \sigma)$ for the demand and equal overage and underage costs of the newsvendor problem, we can easily find the analytical solution which is given by $F(Q) = \frac{c_o}{c_o + c_u}$, where F is the demand cumulative distribution, Q is the order quantity, and c_o and c_u are the overage and underage costs, respectively.

For comparison purposes, we assumed that the overage and underage costs are the same with no holding costs. Table 4 (below) shows the outcomes of the analytical solution and those that emerged from the proposed model. The Mean Absolute Percent Error (MAPE) is less than 0.3% for the simulated case indicating accuracy in finding the optimality neighborhood in simulated scenarios.

Table 4: Comparison between the classical newsvendor and the numerical solutions

μ	σ	Analytical optimal value	Simulation optimal value	# of iterations	%Error
50	10	50	49.98	250	0.0004
100	20	100	100.24	250	0.0024
150	30	150	149.51	250	0.003267
200	40	200	200.56	250	0.0028
50	20	50	50.13	250	0.0026
100	30	100	100.58	250	0.0058
150	40	150	150.61	250	0.004067
200	50	200	199.47	250	0.00265
MAPE					0.2998%

With the above results in mind, we undertake validation of the proposed model using real-life data.

6.3. Analysis 2 (against the five conditions)

The model is validated by utilizing data drawn from the blood platelet inventory of selected hospitals in the State of Kuwait. The data were obtained from publicly available information provided by the Kuwait Central Blood Bank.

The State of Kuwait has a population of nearly three million, although only around 30% of its population are nationals (Central Intelligence Agency, 2019). There are approximately 29 public hospitals and health-related centers in the country, all delivering multi-specialty high-quality care to patients (Kuwait Government Online, 2018). The Kuwaiti Ministry of Health administers all public hospitals, while the Kuwait Central Blood Bank is the main center responsible for obtaining, preserving and safely distributing blood supplies in the country. Although, public hospitals in Kuwait can seek and directly receive donated blood supplies, as the country covers a small geographical area (17,818 km²), the majority of public hospitals source their blood supplies from the Kuwait Central Blood Bank. While platelets may be extracted either following whole blood donation and component separation or directly via apheresis (Williamson and Devine, 2013), the Kuwait Central Blood Bank utilizes apheresis to obtain platelets (Kuwait Central Blood Bank, 2019). Although Apheresis is particularly expensive (when compared to blood component separation), it is generally considered to represent a more superior form of platelet extraction. The use of apheresis to extract platelets is also more likely to ensure that the functional integrity of platelets will not be interfered with during extraction (Burgstaler, 2006; Townsend and Li, 2019). In Table 5 (below), we show the highest observed demand of platelets in selected public hospitals (names have been anonymized) in Kuwait.

As mentioned above, we undertake the analysis on the basis of a period of planning of one calendar year ($T=365$ days). To build higher confidence into the results, each experiment will be repeated a total of 30 times utilizing different random data streams. Using a narrow Half Width HW of \$10 (<5% error margin) for the objective function, thirty replications have been selected as it is a statistically acceptable number to provide good confidence in the results. Following an iterative approach for the first hospital using the expression $HW(R, \alpha) = t_{\frac{\alpha}{2}, R-1} \left(\frac{S}{\sqrt{R}} \right)^2$ (Behnam et al., 2018; Muhammed et al., 2020), where S is the data standard deviation and R is the number of

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replications, the results are shown in Table 6. Of note, since this number will be used for different scenarios, we decided to increase the replications from 28 to 30, although the experiment with 28 replications have yielded a lower number (i.e., 27.07).

Table 5: The demand of platelets' units (selected Kuwaiti public hospitals, 2016)

Hospital	Platelets Aph units	Average daily demand for platelets of different ages (Units/day)				
		<i>Fresh</i>	<i>Young</i>	<i>Mature</i>	<i>Old</i>	<i>Elderly</i>
A	16829	18.4	13.8	6.9	4.6	2.3
B	7164	7.9	5.9	2.9	2.0	1.0
C	5748	6.3	4.7	2.4	1.6	0.8
D	4859	5.3	4.0	2.0	1.3	0.7
E	3084	3.4	2.5	1.3	0.8	0.4
F	2700	3.0	2.2	1.1	0.7	0.4
G	2662	2.9	2.2	1.1	0.7	0.4
H	2526	2.8	2.1	1.0	0.7	0.3
I	2079	-	-	-	-	-
J	1432	-	-	-	-	-
K	368	-	-	-	-	-
L	117	-	-	-	-	-
M	44	-	-	-	-	-

“-” means inapplicable quantity.

“Aph” means Apheresis units.

Table 6: Number of replications.

R	25	28
S	25.503	25.405
$t_{\alpha/2, R-1}$	2.064	2.052
$New R$	27.708	27.176

Four different *Inventory status and issuance policy* scenarios are used in the subsequent experiments. Recall earlier (in section 3.4) that ‘*No-Compatibility*’ referred to a policy where order fulfillment has only exact age match while ‘*With-Compatibility*’ implied where order fulfillment allows for age mismatch. For simplicity of notation, the four scenarios are designated as:

- *Scenario 1* (‘*No-Compatibility-No-Premature expiration*’)
- *Scenario 2* (‘*No-Compatibility-With-Premature expiration*’)
- *Scenario 3* (‘*With-Compatibility-No-Premature expiration*’)
- *Scenario 4* (‘*With-Compatibility-With-Premature expiration*’)

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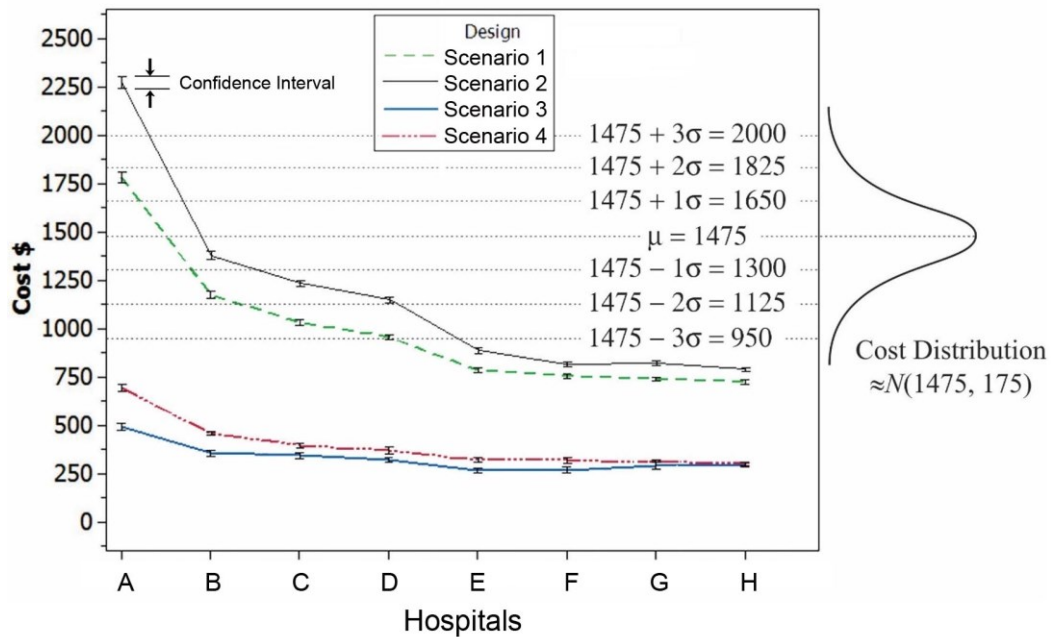
On inspection, it will appear that *Scenario 4* is the most prevalent scenario in realistic applications. It is assumed that the demand for platelets in the eight selected hospitals follows Poisson distribution. Since the demand for blood components is usually discrete and in the form of units, Poisson distribution is applied to model the size of demand occurring within a given time interval. Each occurrence in Poisson distribution is independent of the other occurrences, a fact which coincides with the demand pattern of our model. Since the mean number of occurrences is constant for each specific day, Poisson distribution becomes the distribution of choice. Typically, Poisson distribution is used to model traffic flow and ideal gap distances. Note that both the mean and variance of Poisson distribution are the same. An estimate of the means of the demand associated with each platelet age as reported by each hospital is shown in Table 5. All Kuwaiti public hospitals adhere to JPAC (2019) recommendations for platelet shelf life of five days. For simplicity of designation, we employ the same notation as used during modelling assumptions; that is *Fresh*, *Young*, *Mature*, *Old* and *Elderly*. Table 2 shows the preferences in compatibility when $A=5$.

6.4 Impact of compatibility and premature expiration on cost:

Upon replicating the 4 scenarios above for 30 times, the results were presented in Figure 2. The optimal objective function values of each scenario are detailed to each hospital. Hospitals are ranked in a descending order depending on the level of platelet demands.

What we observe is that the cost of *Scenario 3* is the lowest, followed by *Scenario 4*. While *Scenario 2* exhibits the highest cost, *Scenario 1* comes second highest. The first two scenarios assume that platelets retain their functional integrity until the end of the fifth day in storage. However, the other two scenarios appear more realistic if our contention that premature expiration is an inevitable consequence of storage. Premature expiration has a slight effect on increasing the cost; however, it is the compatibility which has the greatest impact. Indeed, '*With-Compatibility*' will drastically reduce the objective function regardless of premature expiration status.

Figure 2: Average cost/day along with the distribution of the actual cost

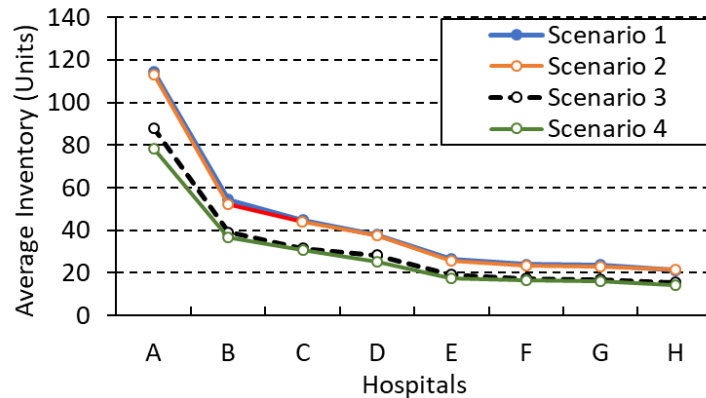


The tight confidence intervals (CIs) in Figure 2 suggest consistent results and a minimum chance of a local minima traps. The mean and standard deviation of the costs were gauged by approximately Norm (445, 53) Kuwaiti Dinars; in effect, Norm (1475, 175) US\$. In Figure 2, this distribution is positioned to show the chances of the actual cost being less than the cost of the proposed policy under the assumption that the actual cost is stochastic, which is extremely unlikely especially when compatibility is allowed. For instance, taking scenario 4 as the most common case under premature expiration of hospital A, the cost is around \$700, hence, this chance will be $\text{NORM.DIST}(700, 1475, 175, 1) = 4.7^{-6}$, that is almost 5 in million times.

6.5 Effect of compatibility and premature expiration on average inventory and inventory mean age:

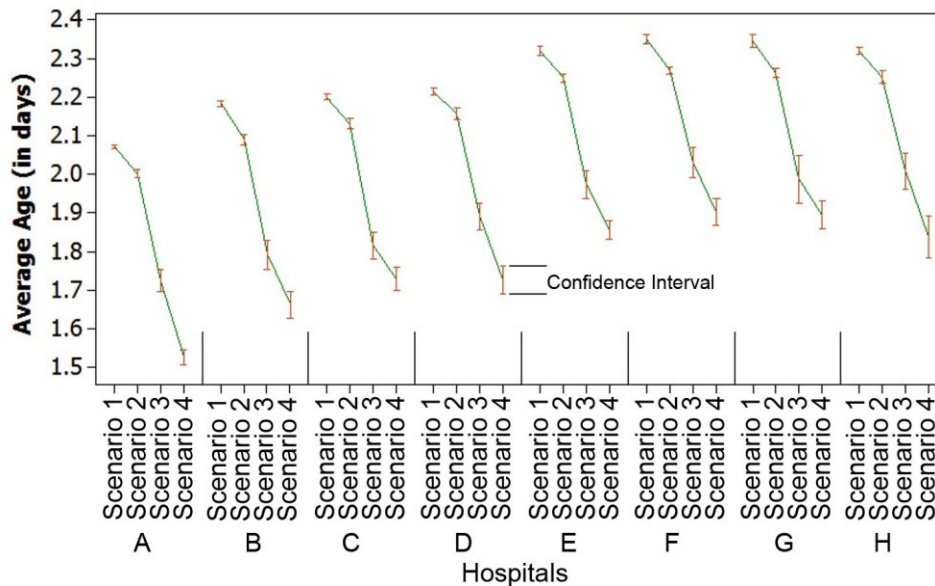
With the descending order of the hospitals with respect to demand, Figure 3 also shows that low demand yields lower average inventory. *Scenario 1* exhibits the highest average inventory, while *Scenario 4* is the lowest, which is a reasonable conclusion since premature expiration reduces the amounts in inventory.

Figure 3: Average inventory (by four scenarios)



Moreover, the variance of the observed average ages increases in the case of the compatibility option. Figure 4 shows the average inventory age detailed to each hospital. The average age decreases by allowing compatibility; yet the confidence interval in Figure 4 increases at the same time.

Figure 4: Average inventory age detailed to each hospital



6.6 The effect of compatibility and premature expiration on the optimal quantities:

In Figure 5 (below), we show for the period of planning of one calendar year ($T=365$ days), the average of ordered platelets for the eight hospitals. As anticipated, it is observed that when substitution is allowed, as an increased number of mismatches are allowed, the quantity of ordered platelets will be less. Nevertheless, slight variations are observed in the ordered quantities between

the four scenarios. This strongly suggests that the inventory policy has an impact on costs. Once again, lower demand entails lower ordered quantities.

Figure 5: Average order quantities of 30 trials

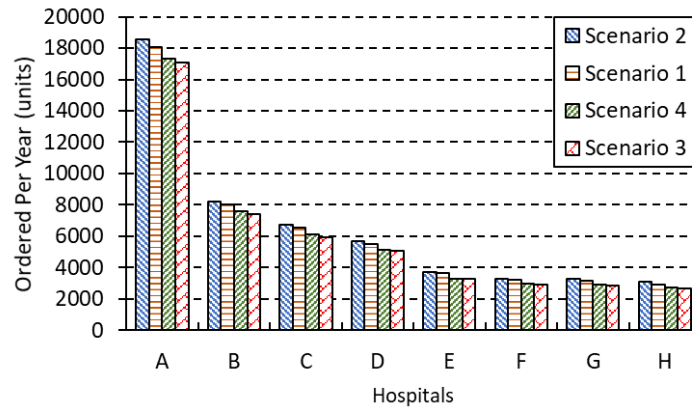
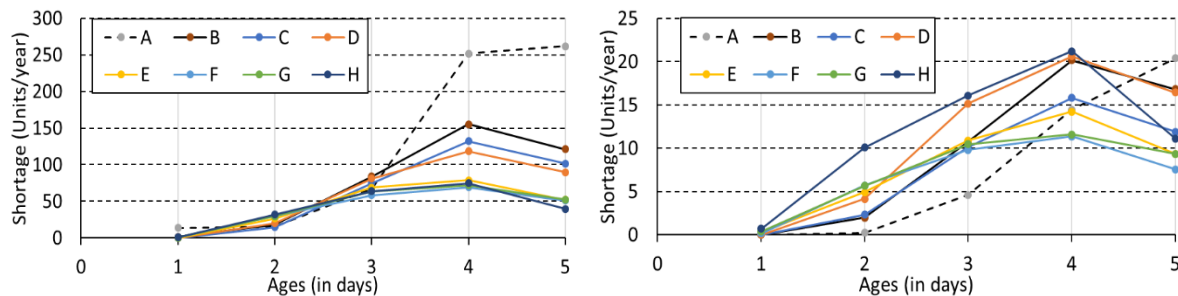


Figure 6-a (below) shows the average shortage for the five ages; from ‘Fresh’ right through to ‘Elderly’, for the case of *Scenario 2*. The average shortage of the five ages for *Scenario 4* is shown in Figure 6-b (below). Clearly, *Scenario 2* presents much higher shortages as only exact match is accepted here. Shortage in ‘Fresh’ platelets will be low because they not only have the highest priority in terms of substitute acquisitions, but also because they are the only platelet types that will receive replenishment. A slight decrease in shortage is observed in the ‘Elderly’ units primarily due to the fact that no subsequent ages will require platelets. Scattered shortage is observed in *Scenario 4* due to induction of premature expiration. While in both scenarios, the shortage tends to increase by age, the impact of compatibility in reducing shortage is significant in every age.

Figure 6: Shortages of *Scenario 2* and *Scenario 4*.

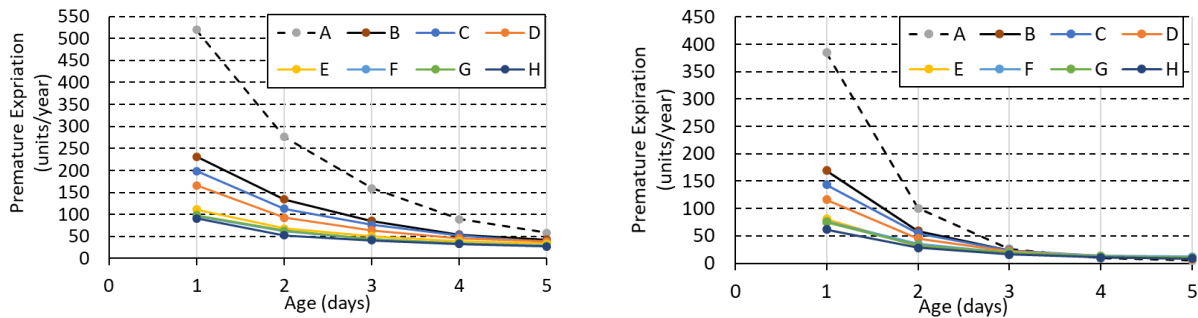


a) For *Scenario 2*, No compatibility but with premature expiration.

b) For *Scenario 4*, With both compatibility and premature expiration.

As for the premature expiration, higher expiration is observed in the case of ‘No-Compatibility’ (Figure 7-a) as compared to ‘With-Compatibility’ (Figure 7-b). This reassures us that compatibility is a key policy in reducing premature expiration cost. Hospitals of higher demands and blood circulation exhibit higher premature expiration (for example, Hospital ‘A’ is the highest, while Hospital ‘H’ is the lowest in both scenarios). Note that with compatibility in Figure 7-b, the premature expiration is lower than that without compatibility.

Figure 7: Premature expiration



a) Premature expiration for Scenario 2

b) Premature expiration for Scenario 4

In Table 7 and Figure 8, we show the outdate quantities for the entire planning period. What we do observe is that hospitals exhibiting lower demands such as Hospital ‘G’ and Hospital ‘H’, experience a lower level of outdates. The problem of outdating is increasingly pronounced in Scenario 1, followed by Scenario 2, Scenario 3 and finally Scenario 4, which presents the lowest outdates.

Figure 8: Outdates in units/year

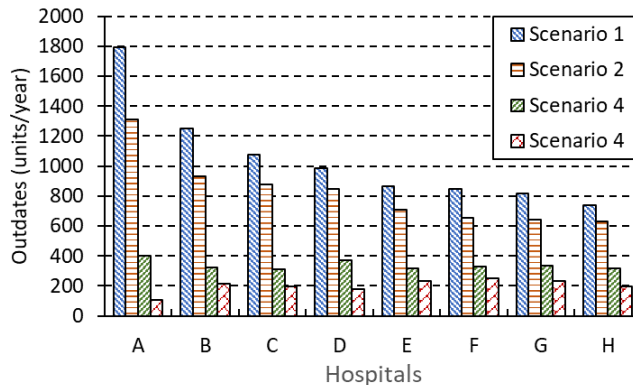


Table 7: The average outdates and their confidence intervals (units/year).

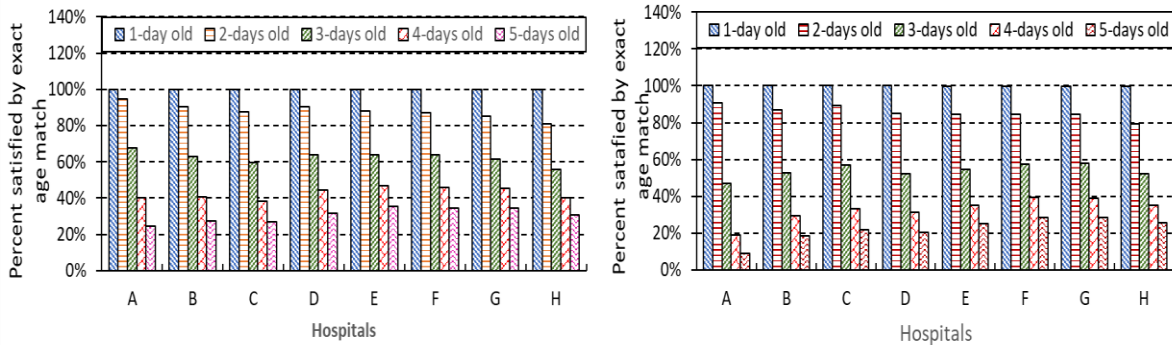
Hospital	Inventory Policy			
	NCNP	NCWP	WCNP	WNWP
'A'	1793.37 [1745.54, 1841.19]	1310.07 [1246.60, 1373.54]	403.57 [359.03, 448.11]	104.87 [90.33, 119.40]
'B'	1251.23 [1222.22, 1280.25]	930.20 [885.49, 974.91]	321.07 [275.55, 366.58]	212.73 [191.46, 234.01]
'C'	1076.23 [1049.81, 1102.65]	879.87 [835.28, 924.46]	313 [273.93, 352.07]	197.40 [178.77, 216.03]
'D'	985.67 [953.32, 1018.01]	846.10 [796.60, 895.60]	371.33 [340.66, 402.01]	179.13 [161.28, 196.98]
'E'	862.53 [835.40, 889.67]	707.33 [683.27, 731.40]	318.17 [288.99, 347.35]	233.47 [218.10, 248.83]
'F'	846.97 [814.79, 879.15]	651.67 [632.87, 670.46]	328.17 [297.35, 358.98]	251.03 [223.06, 279.00]
'G'	814.27 [774.93, 853.61]	639.87 [614.21, 665.53]	336.93 [288.98, 384.88]	231.57 [211.50, 251.63]
'H'	740.87 [721.84, 759.90]	627.90 [591.72, 664.08]	317.20 [273.66, 360.74]	196.40 [166.34, 226.46]

We undertake analysis based on five assumptions – (i) ‘Age-differentiated demand’ (ii) ‘Stochastic demand’ and (iii) ‘Specific inventory issuance policy’. In the present study, five decision conditions will be considered (i) ‘Age-differentiated demand’ (ii) ‘Customized replenishment decisions’ (iii) ‘Custom inventory and order fulfillment policy’ (iv) ‘Different costs considerations’ and most importantly (v) ‘Stochastic inventory expiration lifetimes’. These assumptions are tested against four scenarios.

6.7 Supply-demand Point of Views of different lifetimes

Figure 9 a and b show the percentage of platelets of a specific age that has its demand met by provision of an exact match for *Scenarios 3* and *4*. Of note, the compatibility option means that the demand is satisfied by the exact match first, then a compatible match. Thus, the entire demand for ‘Fresh’ units was fully met by supplying platelets of that age (i.e., 0% of ‘Fresh’ were satisfied by other ages). Approximately 80-95% of the demand for ‘Young’ platelet units was met with an exact match; 55-70% of ‘Mature’ demand was met with an exact match, while 35-45% and 20-35% of ‘Old’ and ‘Elderly’ demand, respectively, were met with an exact match. The demand for older items is satisfied by less exact match. Almost the same percentages are observed in both *Scenario 3* and *Scenario 4*. Except for age “1”, the satisfaction by exact match tends to be lower with premature expiration.

Figure 9: Proportion (%) satisfied by exact match of each age for *Scenario 3* and *Scenario 4*

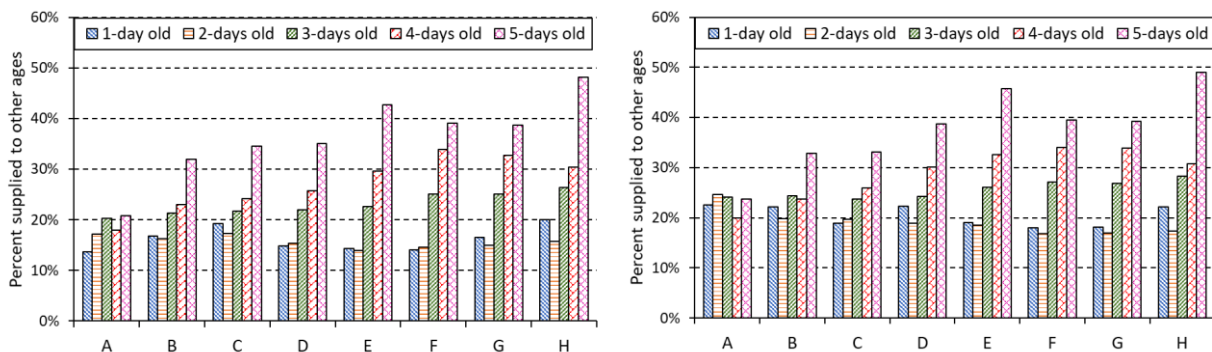


a) Proportion (%) satisfied by exact match against each age for *Scenario 3*

b) Proportion (%) satisfied by exact match against each age for *Scenario 4*

As for the ability to satisfy the demand of platelet units of a specific age with those of another age (in other words, compatibility), Figure 10- *a* and *b* show the percent of each platelet type that was saved to meet the demand of other ages. Note that ‘*Fresh*’ units are not so generous in giving other ages, while ‘*Elderly*’ units (5 days old) participate most in covering other demands. Thus, it will appear that aged (or aging) units do present more opportunities for substitution when compared to those which are younger. By comparing scenario 3 with scenario 4, more generosity in giving can be noticed in the case of scenario 4 due to the increase in scarcity resulting from premature expiration.

Figure 10: Percent used to satisfy other ages

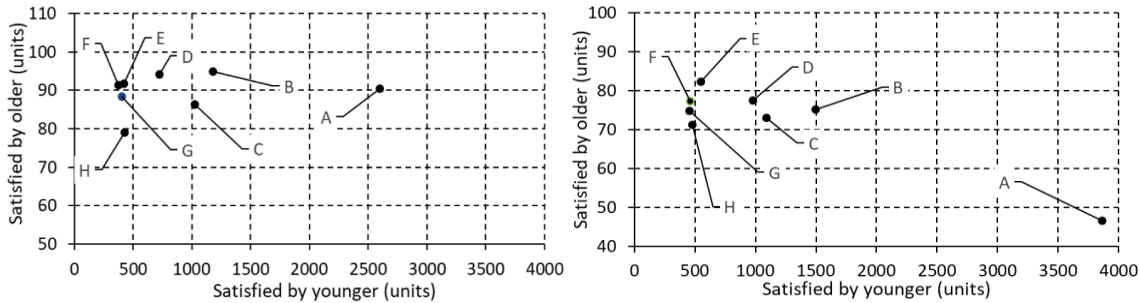


a) Scenario 3 (‘With-Compatibility-No-Premature expiration’)

b) Scenario 4 (‘With-Compatibility-With-Premature expiration’)

Lastly, we consider age mismatch which, as indicated in the literature, does contribute to inventory costs (Haijema et al., 2005; Duan and Liao 2013). To develop a sense on match options, we show in Figure 11-*a* and *b* substitution averages across the eight hospitals.

Figure 11: Substitution averages



a) Average younger versus older substitution for all hospitals against *Scenario 3*

b) Average younger versus older substitution for all hospitals against *Scenario 4*

Clearly, using younger platelet units to meet the demand is prominent in both compatibility scenarios. Recall that satisfying the demand for younger platelets is more desirable than meeting the demand for older ones. Figure 11 hence shows that higher demand results in higher age mismatch of younger platelets, while the magnitude of demand does not have much impact on substitution by older platelets. Compared to *Scenario 3*, *Scenario 4* depends more on substitution by younger platelets. For instance, Hospital ‘A’ has an average of $2600/365=7.12$ units/day satisfied by younger platelets and 0.25 units/day satisfied by older units for the case of *Scenario 3*, while these quantities are 10.6 and 0.13 in *Scenario 4*. Thus, it will appear that hospitals with higher platelet demand increasingly rely on substitution using younger platelets. Further comparison of the two figures shows a wider horizontal spread of the hospitals in scenario 4, which informs that higher numbers of orders is satisfied by younger ages due to experiencing premature expiration.

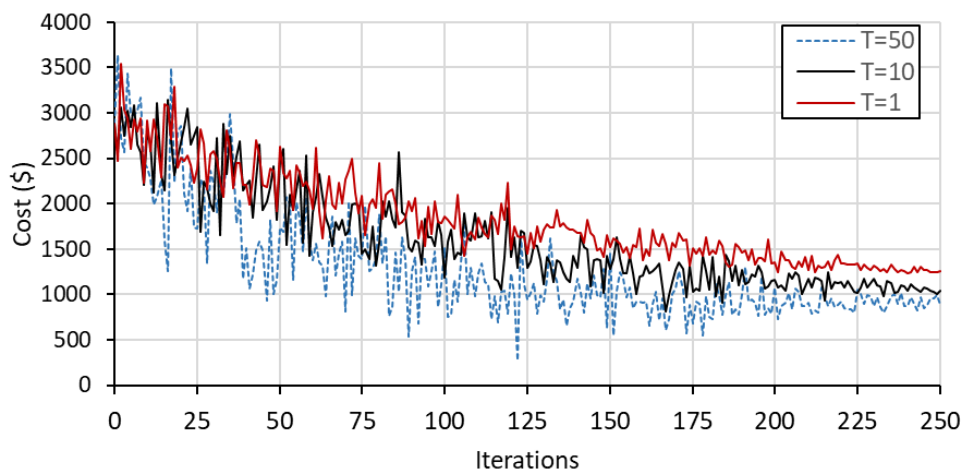
7.0 Sensitivity Analysis

The experimental part above presents different scenarios for different hospitals each of its own input. The different scenarios show the robustness of the model and its ability to cope with different

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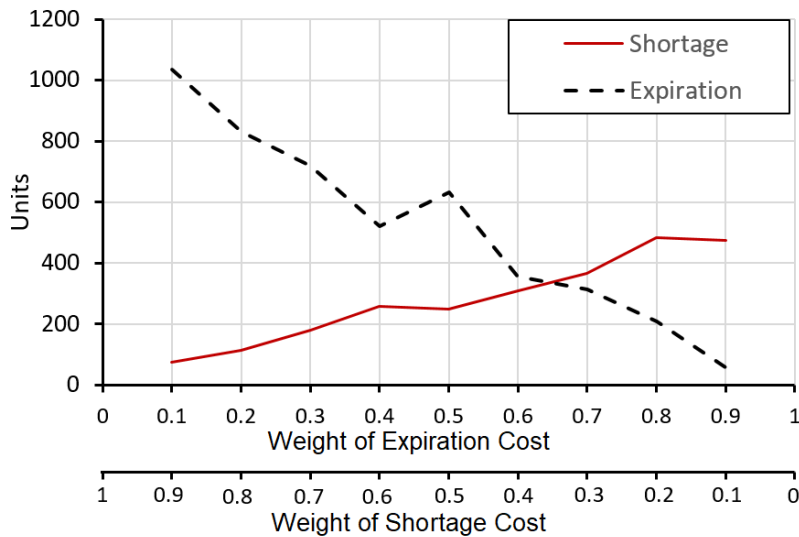
demand patterns. For further sensitivity analysis, we show the convergence of the search algorithm given different initial temperatures of SA. Figure 12 shows the objective function vs. the number of runs being tested while searching for the best solution for the case of hospital ‘A’ where, $\alpha = 0.9$, $\theta = 0.5$. Clearly, higher temperatures could demonstrated lower costs, however with higher oscillations due to higher ability to skip local optima (the bottom line). On contrary, low temperatures result in less flexibility while searching the solutions’ neighborhoods and higher cost with less oscillations.

Figure 12: The valuation of the cost function vs. different iterations.



Similarly, by conducting experiments to test the effect of weighted costs, acceptable results could be found in Figure 13. The expiration and shortage costs were considered for the tradeoff between the two components for hospital ‘E’. When the cost of expiration is emphasized, low number of outdated units is observed while the shortage tends to increase due to its low cost. The opposite pattern can be observed where low shortage and higher expiration are observed for high shortage and low expiration weights. In our model general settings, the shortage cost is higher than the expiration cost which explains the high expiration compared to shortage.

Figure 13: The results of weighted shortage and expiration costs for hospital “A”.



Finally, while to a certain extent age matching is employed in practice, particularly for patients who require exact ages as illustrated in section 1 and 2, the current practice does not consider systematic order fulfillment policies, resulting in inefficient inventory management. By employing the presented procedure for order fulfillment along with the resulting optimal quantities, costs can be reduced. It is important to note that blood is collected in custom-manufactured 500ml packs, while the resulting optimal quantities may have fractions due to continuous solution space. This may bring some practical difficulties in the implementation. Moreover, restricting the optimal quantities to integer numbers may result in worse solutions. As for premature expiration, the common practice does not include real-time monitoring of blood components, where tests are conducted only upon the inquiry of the quantities. Research is continuing on the issue of real-time monitoring of blood condition and the level of deterioration/contamination. Anyway, the proposed model is promising in terms of cost reduction due to shortage, outdating, random expiration and age differentiated demand. Lastly, the order fulfillment guidelines can be easily programmed in digitally monitored storage chambers.

8. Conclusions

As in the case of the wider operations and supply chain management arena, the need for optimal use of very limited products and services is essential to the healthcare services industry. The

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implications of this is that the use of simulation is now been widely utilized to address healthcare management challenges – one such challenge to which this study focuses upon is the need to minimize volatility in blood platelet supply and demand. Doing so will arguably not only save lives, but also ensures that the wider society is not exposed to contaminated blood supplies.

The context of blood supplies has retained considerable research interest among scholars. Noting a substantial amount of literature on deterministic lifetimes of blood as perishable inventory, but paucity in the studies on randomized *accelerated* deterioration, this study set out with the assistance of a simulation and optimization inventory management model, to explore how best to mitigate against inventory volatility in blood platelet. The study was set against five decision conditions, some like ‘*Customized Replenishment decisions*’, ‘*Inventory status and issuance policy*’ and ‘*Different costs considerations*’ have been prominently articulated in the academic literature, while others such as ‘*Random aging and age-differentiated demand*’ and ‘*Random inventory expiration lifetimes*’ appear to have been hardly explored. Utilizing data drawn from the blood platelet inventory of selected hospitals in the State of Kuwait, analysis was undertaken in the form of tests set against different *inventory status and issuance policy* scenarios. Findings from the study suggested that conditions where higher quantities of perishable products stocked in inventories will lead to experiencing premature expiration. Findings also suggests that in perishable inventories, higher levels of shortages and premature expiration will be experienced where there is an absence of product compatibility (substitution). Other findings suggested that older perishable products appeared to enjoy a higher likelihood of compatibility (substitution). Conversely, newer perishable products were more likely to be age-specific, and thus experience less compatibility (substitution). Taken together, this study is one of the very few that has addressed two relatively explored decision conditions in perishable inventory management, that is, ‘*Random aging and age-differentiated demand*’ and ‘*Random inventory expiration lifetimes*’. The reality that inventory management decisions may be dependent on these conditions should no longer be disregarded and should be of interest to future research.

In order to best determine the quantity of platelets to order, the number to replenish, orders to be fulfilled, when and which platelets to be utilized to meet demand, operations managers require a full and comprehensive picture of inventory levels and patterns. This is because more often than

not, platelets of different ages are stored on the same shelf. Without this information, the successful management of platelet inventory becomes extremely challenging and near impossible. Arguably, the findings from the study serves as an appropriate platform to advance implications for operations management practice. The first being the desire for healthcare service provider to focus their attention on *accelerated* degradation and deterioration as assessed by both expiration due to *aging* and *premature expiration* of stored platelets. Apart from visual inspection (which requires experience), it may be possible to detect such early degradation and deterioration (expiration) through proactive screening (see Dreier et al., 2008). In essence, the management of platelet inventories requires constant inspection and monitoring. The versatility of the developed solution allows for its use and application beyond the realms of perishable inventory management in healthcare services settings. Certainly, the authors acknowledge that, to generalize the outcomes of the study, the model requires to incorporate scenarios and regulatory environments which differ not only across countries, but also between different healthcare settings. Nevertheless, the study does provide a firm foundation to allow managers from other industry sectors to apply this solution in order to enhance the management of their perishable inventories. This is possible because the decision conditions that served as the foundation for the study is not specific to the case. Instead, these conditions were derived from a wide review of perishable inventory literature. In effect, the five conditions can be used as decisional means to improve the performance of perishable inventories in other service environments such as the pharmaceutical industry where drug expiration of branded products remains a key challenge.

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