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Reducing the age of transfused red blood cells in hospitals: ordering and allocation policies

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Running title: Reducing the issue age of blood in hospitals

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Background: Although recent randomized controlled trials have not found increased risk of morbidity/mortality with older Red Blood Cells (RBCs), several large trials will be completed soon providing power to detect smaller risks if indeed they exist. Hence, there may still be a need for inventory management policies **that** could reduce the age of transfused RBCs without compromising availability or resulting in excessive outdates.

Materials and Methods: We developed a computer simulation model based on data from an acute care hospital in Hamilton, Ontario. We evaluated and compared the performance of certain practical ordering and allocation policies in terms of outdate rate, shortage rate, and the distribution of the age of issued RBCs.

Results: During the **one** year period for which we analyzed the data, 10,349 RBC units were transfused with an average issue age of 20.7 days and 6 units were outdated (outdate rate: 0.06%). Adopting a strict first in, first out (FIFO) allocation policy and an order-up-to ordering policy with target levels set to 5 times the estimated daily demand for each blood type, reduced the average issue age by 29.4% (to 14.6 days), without an increase in the outdate rate (0.05%) or resulting in any unmet demand. Further reduction of issue age without a significant increase in outdate rate was observed when adopting non-FIFO threshold-based allocation policies and appropriately adjusting the order-up-to levels.

Conclusion: A significant reduction of issue age could be possible, without compromising availability or resulting in excessive outdates, by properly adjusting the ordering and allocation policies at the hospital level.

Key words: Inventory management, Red Blood Cells, Simulation.

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Introduction

A substantial body of literature [1] suggests an association between transfusion of older Red Blood Cells (RBCs) and adverse clinical outcomes for transfused patients. Recent Randomized Controlled Trials (RCTs) could not show an increased risk of harm for premature infants [2], cardiac surgery patients [3] and critically ill adults [4]. The results are however not conclusive, due to limitations and possible design issues of the RCTs [5-6]. The results of four ongoing RCTs [7-10] enrolling a total of 40,835 patients are yet to be published and collectively they will have sufficient power to detect even smaller difference in mortality (1-1.5%), if indeed such a difference does exist. Even these small differences would be of clinical relevance given that transfusion is one of the most frequently used medical interventions. Therefore, in anticipation of the results confirming the adverse outcomes of "older" RBCs, it is imperative to be equipped with inventory policies that could reduce the age of transfused RBCs without compromising availability or resulting in excessive outdates.

Previous studies have investigated the impact of reducing the shelf-life of RBCs (42 days) at the hospital level [11] and on regional blood supply chains [12-13]. However, less attention has been given to alternative inventory management policies **aiming to reduce the age of transfused RBCs**. In a simulation study, Atkinson et al. [14] investigated the potential of a family of threshold-based allocation policies in reducing the age of transfused RBCs without jeopardizing RBC inventory availability. The policy was further explored using a theoretical approach by Abouee-Mehrizi et al. [15]. Both studies treat the supply of blood to the hospital as exogenous and hence do not consider ordering policies within the hospital. However, RBC units in hospitals are typically ordered from a central supplier. By changing their ordering policy, hospitals can control the amount of RBC inventory on hand, which in turn affects the age of units at the time of issue for transfusion.

The aim of our study is to assess the performance of practical ordering and allocation policies in reducing the age of transfused RBCs while keeping the outdate and shortage rates low. We built a simulation model based on data from an acute care teaching hospital in Hamilton, Ontario. We then used the simulation model to estimate and compare the outcomes of various policies.

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Materials and methods

Study design

We developed a computer simulation model based on the RBC inventory of an acute care teaching hospital in Hamilton, Ontario. We used historical data from 2011 to validate the model and estimate its inputs. For a given allocation and ordering policy, the model estimates the annual outdate rate, shortage rate, and the distribution of the age of RBCs at the time they are issued for transfusions (referred to as issue age in this manuscript). Using the model, we evaluated and compared the outcome of several ordering and allocation policies when satisfying the same historical demand as observed in 2011. The outputs were compared with the historical data as a benchmark. The study was approved by the Hamilton Integrated Research Ethics Board.

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Data

We used transaction-level records for RBC inventory of the hospital to validate our model and estimate its required inputs. Data were extracted from the Transfusion Registry for Utilization, Surveillance, and Tracking (TRUST) database, a prospective hospital-based registry of all patients admitted to acute care hospitals in Hamilton, Ontario. We used records for all RBC units (hereafter referred to as units) received by the hospital in 2011, which amounted to a total of 10,411 records. Each record corresponded to a single unit and included the: ABO/Rh type of the unit; date the unit was collected from the donor by Canadian Blood Services (CBS); date the unit was received by the hospital; the final disposition of the unit (transfused, expired, etc.) and the date that final disposition occurred; and, the ABO/Rh type of the patient receiving the unit.

Simulation model

Simulation procedure

We developed and implemented our simulation model in R [16]. The simulation model has 4 main parts, briefly described below.

1. **Initialize.** At the beginning of the simulation, the inventory was initialized by setting the number of available inventory for each blood type and the initial age of each unit.

2. **Replenish inventory.** At the beginning of each simulation cycle (corresponding to a day) the inventory was replenished for each blood type according to the ordering policy. We assumed that the orders were fully satisfied.
3. **Satisfy demand.** The demand for the day was realized one-by-one and satisfied (if possible) according to the allocation policy and the ABO/Rh substitution rule. Any demand that could not be satisfied using the inventory on-hand was assumed to be satisfied using an emergency order and was counted as unmet demand (shortage).
4. **Update inventory.** At the end of the simulation cycle, the age of all units in inventory were increased by 1. All units exceeding the shelf-life were removed from the inventory and counted as outdated.

Trace-driven simulation

We implemented a trace-driven simulation by setting all inputs of the simulation model according to the historical data. That is, for each day *i*, the inventory was replenished with units that had receipt date equal to *i* and with the same receipt age observed in the data; demand was set to all units which were transfused on day *i*; and the units were allocated to the demand exactly as observed in the data. This way, we were able to observe the state of the inventory (count and types) each time a unit was transfused. The trace-driven simulation **was used to identify the current ordering and allocation policies of the hospital, as explained below.**

Model inputs

The model has two types of inputs; fixed and controlled. Fixed inputs were estimated or directly set using the data and kept identical in all scenarios. Controlled inputs varied among different scenarios. Since the objective of our study was to evaluate the outcome of alternative ordering and allocation policies, they were set as the controlled inputs. We also modeled the current ordering and allocation policies of the hospital. The resulting model is called the "baseline scenario" and its performance was compared to the historical data.

Initial inventory. The initial inventory was obtained using data for 2010. Specifically, the inventory was initiated by identifying and calculating the age of all units which were received by the hospital in 2010 and their final disposition occurred in 2011.

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Initial age of units. Since the number and type of units that are received by the hospital are affected by changing the ordering and/or allocation policy of the hospital, we could not directly use the data for this input. Instead, we used the data to obtain the empirical distribution of the age of units at the time of receipt by the hospital for each blood type. When replenishing the inventory, we simulated the receipt age by randomly drawing from these empirical distributions. The receipt age distribution is illustrated in Figure 1. The receipt age was between 2 and 40 days with an average of 10.4 days, a median of 9 days and a standard deviation of 5.4 days. Note that we ignore the potential effect of adjusting the ordering and allocation policies on the age of supplied blood to the hospital (see also the Discussion section).

Demand. Daily demand data for 2011 was directly used as the demand input in the simulation model. The average daily demand was 28.6 units with standard deviation of 12.2. The daily demand fluctuated considerably during the year with a maximum of 76 units observed in November, and a minimum of 6 units in August.

Other final dispositions. Beside transfused and outdated units, there were also a few units that were discarded for storage deviations (issued and returned outside of the allowed time frame) or transferred to another hospital. These events were taken into account directly using the data. For example, if a unit was contaminated on January 1st, in the simulation model a unit of the same type and age was randomly selected and removed from the inventory in the first simulation cycle.

Emergency/trauma cases. Using the trace-driven simulation we identified 769 instances where a compatible but not an ABO or Rh specific unit was substituted for an exact match. For 689 of these cases an exact match was available in the inventory. The majority of these cases corresponded to substitution of O– and O+ types, suggesting that the demand points were associated with emergency or trauma cases. We flagged these demand points in all scenarios and forced the model to allocate the same type observed in the data. If that specific type was not available in inventory, the demand was counted as unmet.

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Allocation policy. We observed that the hospital did not strictly follow a FIFO policy. In particular, among 10,349 transfusions, there were 8709 (84%) instances where an older unit of the same type was available in the inventory. Nevertheless, in the majority of cases older units were allocated with a higher probability especially if there were units in the inventory that had a short remaining shelf-life. We also analyzed how ABO/Rh compatible units were substituted in cases where the demand could not be satisfied using an exact match. There were 80 instances where an exact match was not available in the inventory. We analyzed these cases and identified the substitution rule (data not displayed). To model the allocation policy of the hospital in our simulation, after selecting the type of the unit to be allocated (by giving preference to an exact match and using the substitution rule if an exact match was not available) one unit was randomly selected from the n oldest units, except if the oldest unit was older than Z days. In the latter case, the oldest unit was allocated. We then estimated the parameters to be $n = 8$ and $Z = 34$ using the data.

Ordering policy. The hospital used order-up-to levels for each blood type to replenish the inventory on a daily basis from Monday to Saturday. That is, at the end of each day, an order was placed to replenish the inventory up to the order-up-to levels. Non-routine orders were also made if the inventory level of any blood type was "too low". In the data we could not observe the type of orders. Therefore, we used the average inventory-on-hand at the beginning of the day as order-up-to levels for each blood type.

Validation

We conducted 30 simulations of the baseline scenario and compared the average output with historical data. The average issue age and the number of transfusions for each blood type are compared with data in Table 1. The aggregate distribution of the issue age (across all types) obtained from the simulation is also compared with the empirical distribution in Figure 2. Results indicate that the simulation outputs are in close agreement with the historical data in terms of the issue age. The average number of outdates across simulations was 13.9 units (standard deviation: 3.27), which is higher than the actual number of outdates in 2011 (6 units). However, this difference (which is less than 0.08% of total units) can be attributed to our simplified model of the hospital ordering policy that does not include more flexible practices

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such as emergency orders. Overall, minor discrepancies between the simulation and reality are expected as the ordering and allocation policies followed by the hospital are not as systematic as modeled in the simulation. Nevertheless, the proposed model seems to adequately capture the main features of the hospital RBC inventory and hence is useful in evaluating the effect of alternative (and more systematic) ordering and allocation polices.

Policies

We considered a threshold-based allocation policy similar to the one suggested by Atkinson et al. [14] and varied the threshold value across scenarios. Under a threshold policy with parameter T, upon receiving a demand, first the type of blood to be allocated is selected in the order specified in Table 2 (also used in Simonetti et al. [17]). Next, the oldest unit of the selected type that is younger than the threshold T is allocated. If all units of that type are older than T, the freshest unit available is allocated. For $T = 42$ the policy always allocates the oldest unit and hence is equivalent to FIFO. For $T = 0$ the policy always allocates the freshest unit and hence reduces to LIFO. **(See the Supplementary Material for illustrative examples.)**

In all scenarios the ordering policy was to replenish the inventory level on a daily basis (except Sundays) to specified order-up-to levels for each blood type. We considered 4 different ordering policies by varying the order-up-to levels. Specifically, we considered the current ordering policy (i.e., with order-up-to levels set to the average inventory level for each type, which was approximately 10 times the daily demand) in addition to the alternatives of keeping 7, 5, and 3 times the average daily demand in the hospital. For each of the four ordering policies, we considered 6 allocation policies by setting the threshold value to $T = 42$, 28, 21, 14, 7, and 0. We then simulated each of the 24 scenarios and compared their performances.

Results

Trade–off between the average issue age and the outdate rate

The output of scenarios were compared to the historical data in terms of the resulting issue age, proportion of outdated units and the proportion of unsatisfied demand. No unsatisfied demand (shortage) was observed under any of the allocation policies when 5 or more days of inventory was kept (data not shown). When the policy was to keep 3 days of inventory, a small proportion

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of demand was unsatisfied (maximum 0.65% for LIFO). Figure 3 illustrates the trade-off between the average issue age and proportion of outdates across all scenarios. Note that each line corresponds to a specific ordering policy, and the tick marks on each line correspond to different allocation policies under that ordering policy. Thus, the figure presents the joint effect of the ordering and allocation policies. Comparing to the historical data (average issue age: **20.7** days, outdate rate: 0.06%), by adopting a strict FIFO policy ($T = 42$) and keeping 7 or 5 days of inventory, the average issue age is reduced by 19.9% (to 16.6) and 29.4% (to 14.6), respectively. This is achieved without an increase in the outdate rate (0.06% for 7 days of inventory and 0.05% for 5) and without resulting in any unmet demand. By adopting a FIFO policy and keeping 3 days of inventory, the average issue age is reduced by 38.3% (to 12.7), again without an increase in the output rate (0.05%) but leading to 0.64% of unsatisfied demand.

Further reduction of average issue age for each of the ordering policies is observed under alternative allocation policies (lower threshold values). This is however achieved at the cost of an increased outdate rate. When inventory levels are high, both the reduction of average issue age and the increase in outdate rate are more significant (Figure 3). Under current inventory levels, following a threshold policy leads to unacceptably high outdate rates (e.g. 18% for $T = 14$). With lower inventory levels the increase in output rate is smaller, but at the same time the reduction of average issue age is less significant. When the threshold value is 7, the performance is very close to that of LIFO for all ordering policies.

We note that the inventory policies did not lead to an increased number of Rh incompatible transfusions compared to the historical data. In all simulation scenarios Rh incompatible transfusions were below 0.9%. (See Supplementary Table S1.)

Distribution of the issue age

We also evaluated the policies in terms of the resulting issue age distribution. The results for selected scenarios are presented in Figure 4. The empirical distribution of issue age obtained from data is also presented. The empirical distribution has a higher fraction of "older" units (e.g., above 28 or 35 days) compared to alternative scenarios including the ones with FIFO allocation policy. Non-FIFO allocation polices significantly reduce the fraction of units with issue age

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above the threshold, as they only issue units with age above the threshold as a recourse action. An exception is when $T = 7$. This is because about 67% of units have age higher than 7 at the time of receipt by the hospital (see Figure 1). For higher threshold values, however, the majority of units have issue age below the threshold, especially when high levels of inventory are kept. This is illustrated in Figure 5. Observe that with current levels of inventory a significant majority of issued units have age below the threshold (**except** when $T = 7$). When the ordering policy is to keep 3 days of inventory, a higher proportion of units have age above the threshold under each allocation policy.

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Discussion

Our analysis revealed that the hospital did not strictly follow a FIFO policy. In contrast, we observed that the allocated units were among the "older" units available in the inventory. We speculate that this is due to current hospital policies where fresh blood is selected for neonates and for alloimmunized patients who require RBCs with a specific phenotype. Upon receiving a request for RBCs, it is also possible that the RBC units retrieved from the front of the fridge, where the older units are typically kept, are in fact misplaced in order of dating, resulting in a situation where the *oldest* available unit is not being issued for transfusion. Regardless of the exact reason, we found that while this deviation from FIFO policy had little effect on the average issue age, its impact on the distribution of issue age was significant. In particular, it resulted in significantly higher proportion of units older than 28 days compared to a strict FIFO policy.

We observed that by following a strict FIFO policy and lowering the order-up-to levels, the hospital could significantly reduce the average issue age. The reduction of average issue age was achieved without resulting in unsatisfied demand or increasing the outdate rate, suggesting that the hospital inventory levels were unnecessarily high.

Further reduction of the average issue age was observed under different threshold policies. The threshold policy was particularly effective in limiting the proportion of units older than the threshold. Nevertheless, it was observed that the trade-off between the average issue age and the outdate rate highly depends on the ordering policy. In particular, with high levels of inventory the increase in outdate rate was unacceptably high. This could be explained using our results on the distribution of issue age. Under a threshold policy with parameter *T*, units with age above *T* are only issued when there are no units available below that age. With high levels of inventory (e.g., 7 times the average daily demand), the availability of units with age below the threshold is high (an exception is when *T* is very small e.g. 7 which we shall discuss shortly). The excess inventory with age above *T* is therefore mostly not used and eventually expires. In contrast, with lower levels of inventory, a lower proportion of units have age above the threshold but a higher proportion of allocated units are among such units. As a result, the added outdate rate is smaller, yet the reduction of average issue age is less significant. When the threshold value was small (e.g., equal to 7) the performance of the threshold policy was close to LIFO. The reason is that about 67% of units were already older than 7 days when delivered to the hospital. Therefore, even when large amounts of inventory were kept, the majority of issued units had age above 7 days. Since under the threshold policy the freshest unit is issued if there are no units younger than the threshold, the policy results in approximately the same performance as LIFO.

Our study has some limitations. We evaluated the policies in meeting the same demand as observed in the historical data. Robustness of our results to different demand profiles should therefore be investigated in future. We also assumed that the hospital orders are fully satisfied. In reality the orders may be partially satisfied if the supplier is facing a shortage. Nevertheless, our study provides insights and quantifies the impact of inventory levels on the outdate rate, issue age and availability of RBCs. Further, it appears to be the first to investigate the joint effect of ordering and allocation policies on the age and availability of RBCs.

The threshold-based allocation policy considered in this paper slightly differs from that suggested by Atkinson et al. [14]. In particular, our threshold policy allocates units differently when an exact match is not available. Our policy first chooses a compatible type according to Table 2, and then allocates the oldest unit of that type which is younger than the threshold. In contrast, their policy allocates the oldest unit among all compatible units that are younger than the threshold. While simulation results revealed no significant difference between the outcomes of these policies (data not shown), our policy seems to be more practical as it could be easily implemented by dividing the shelf for each blood type into two categories (younger and older

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than the threshold) and it does not require information on the age of all units in the inventory. Further, as our policy prioritizes choosing a compatible type, it reduces the number of Rh incompatible transfusions.

Our results on the performance of the threshold policy also differ from those reported by Atkinson et al. [14]. They estimated that by using a policy with a threshold of 14 days, the average issue age can be reduced by 10 to 20 days while increasing the proportion of unmet demand by 0.05% (outdate rate not reported). Our study predicts a less significant reduction of issue age and identifies the potential risk of increased outdate rate under the threshold policy when inventory levels are high. The discrepancy can be linked to the modeling assumptions, in particular those on the supply side. In their model, RBC units arrive at the hospital one-by-one according to a random process. More importantly, all units are 2 days old when entering the hospital inventory. In our model, inventory is replenished according to an order-up-to policy and the initial age of units is randomly drawn from an empirical distribution. Our assumptions are more representative of the operations of hospitals that order their required blood from a central supplier.

Our study identifies a potential in reducing the age of transfused RBCs through practical inventory policies at the level of hospitals. Future work should investigate the effect of the size of the hospital, frequency of deliveries to the hospital, and alternative ordering and allocation practices on the issue age and availability of RBCs. Furthermore, a broader study of the blood supply chain is required to understand the effects of adjusting inventory policies at a group of hospitals sharing the same supplier. For instance, we assumed that modifying the ordering policy does not affect the initial age of units at the time of receipt by the hospital. However, reduction of inventory levels at a group of hospitals in the region, could affect the initial age of units due to an increased level of inventory at the supplier level. In this case, the supplier should accordingly modify its inventory policies to balance the risk of shortage and the age of supplied units to the hospitals. It should however be noted that following a systematic ordering policy at the hospitals is expected to reduce the demand variability for the supplier and allow it to better manage its inventory.

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Figure and Table Legends

Figure 1: Distribution of the age of units at the time of receipt by the hospital.

Figure 2: Issue age distribution obtained from simulation (baseline scenario) compared to the empirical distribution obtained from data.

Figure 3: Trade-off between average issue age and proportion of outdates under different ordering and allocation policies. Each line corresponds to the specified ordering policy. The tick marks on each line (from left to right) correspond to allocation policies with $T = 42$ (FIFO), 28, 21, 14, 7, and 0 (LIFO). The symbol (×) marks the performance of the hospital in 2011 obtained from the data.

Figure 4: Issue age distribution for selected allocation policies when keeping (a) current levels of inventory, (b) 5 days of inventory and (c) 3 days of inventory.

Figure 5: Fraction of units issued with age below or above the threshold under selected allocation policies when keeping (a) current inventory levels and (b) 3 days of inventory.

Table 1: The output of simulations (baseline scenario) versus data.

Table 2: ABO/Rh compatibility in order of preference used in simulation scenarios.

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Table 1 The output of simulations (baseline scenario) versus data

Average Issue age						Number of units transfused				
Product	Data	Simulation		Relative error		Data	Simulation		Relative error	
		Mean	SD	Mean (%)	SD (%)		Mean	SD	Mean (%)	SD (%)
A+	20.78	20.54	0.07	1.14	0.32	3371	3406.9	0.07	1.08	0.27
A-	21.78	21.44	0.20	1.68	0.65	691	685.7	0.20	2.03	0.60
B+	27.23	27.31	0.24	0.77	0.45	789	784.5	0.24	0.58	0.16
B-	17.17	17.73	0.31	3.28	1.71	139	136.9	0.31	1.99	1.20
AB+	25.63	25.15	0.62	2.47	1.79	253	228.9	0.62	9.68	3.46
AB-	24.75	22.10	1.21	10.71	4.88	32	33.6	1.21	5.12	2.14
O+	19.03	18.96	0.07	0.43	0.33	4032	4029.6	0.07	0.10	0.07
O-	19.97	20.11	0.12	0.78	0.45	1042	1042	0.12	0.50	0.29
All types	20.66	20.52	0.06	0.67	0.27	10349	10349	-	0.00	-

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Table 2 ABO/Rh compatibility in order of preference used in simulation scenarios

Demand blood type	Compatible types in order of preference							
	First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth
A+	A+	O+	A-	O-				
A-	A-	O-	A+	O+				
B+	B+	O+	B-	O-				
B-	B-	O-	B+	O+				
AB+	AB+	A+	B+	O+	AB-	A-	B-	O-
AB-	AB-	A-	B-	O-	AB+	A+	B+	O+
O+	O+	O-						
O-	O-	O+						

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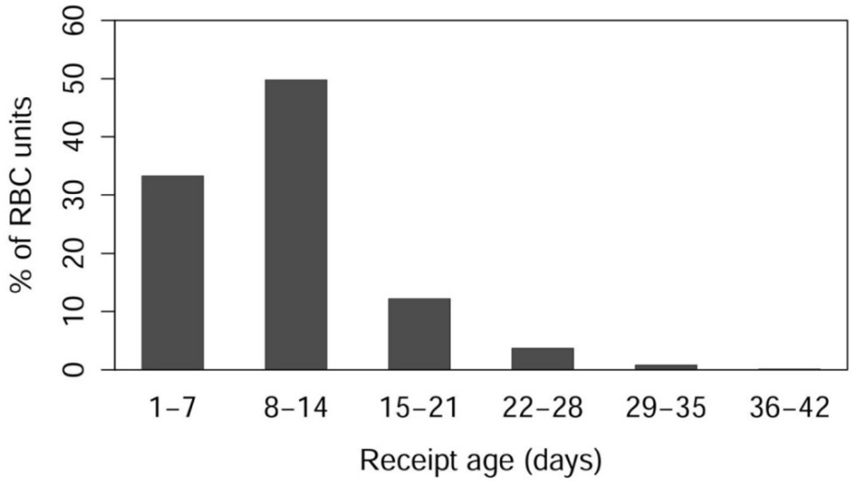

Figure 1: Distribution of the age of units at the time of receipt by the hospital.

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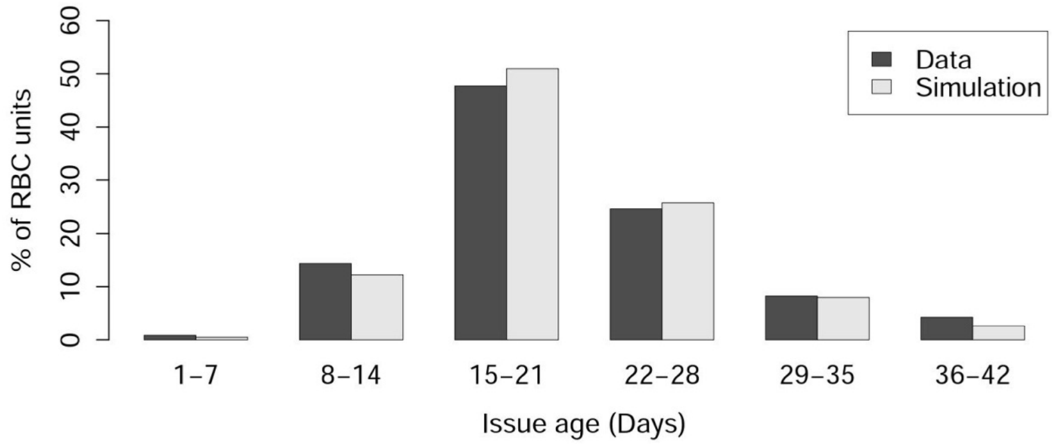

Figure 2: Issue age distribution obtained from simulation (baseline scenario) compared to the empirical distribution obtained from data.

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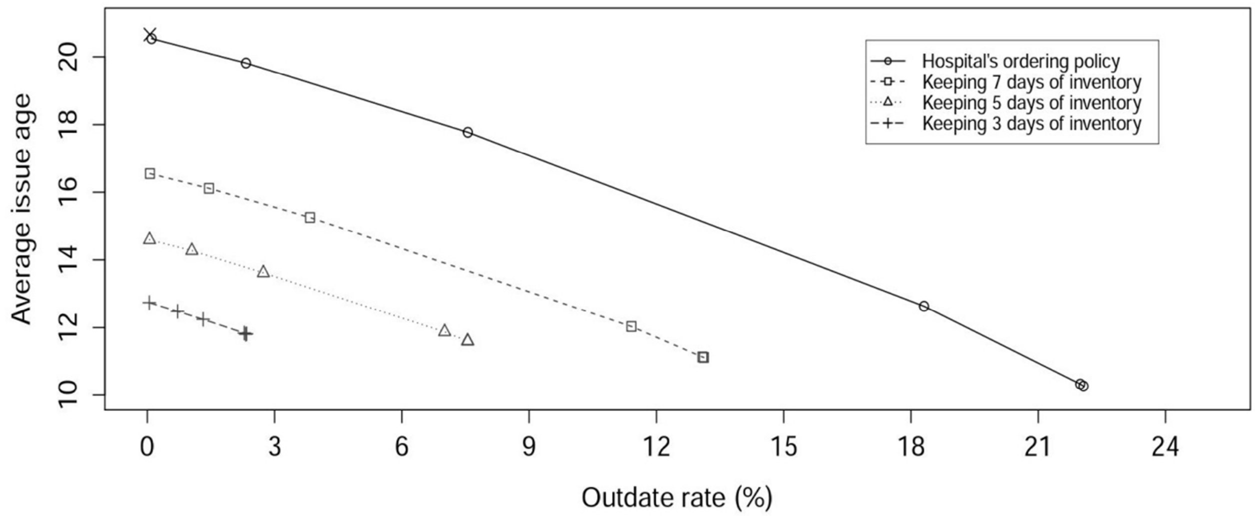

Figure 3: Tradeoff between average issue age and proportion of outdates under different ordering and allocation policies. Each line corresponds to the specified ordering policy. The tick marks on each line (from left to right) correspond to allocation policies with T = 42 (FIFO), 28, 21, 14, 7, and 0 (LIFO). The symbol (×) marks the performance of the hospital in 2011 obtained from data.

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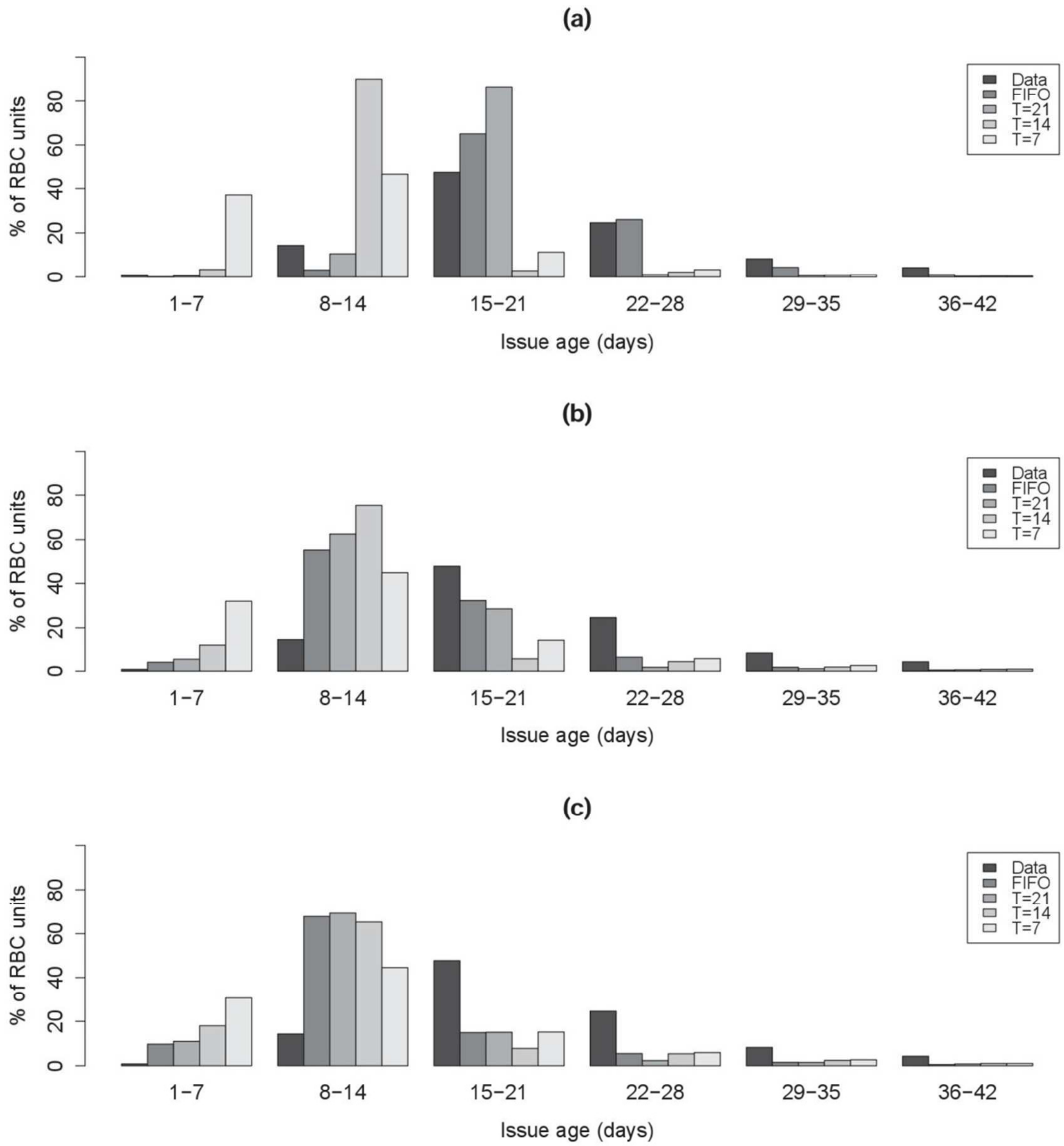

Figure 4: Issue age distribution for selected allocation policies when keeping (a) current levels of inventory, (b) 5 days of inventory and (c) 3 days of inventory.

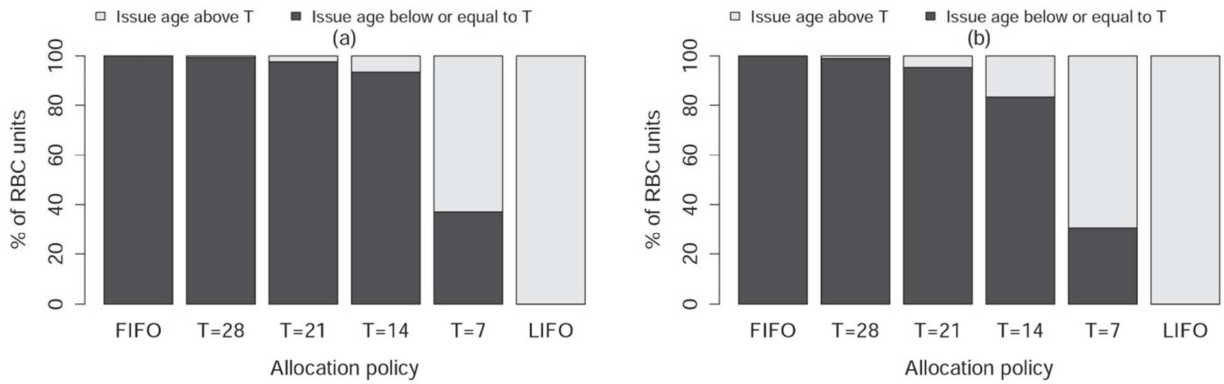

Figure 5: Fraction of units issued with age below or above the threshold under selected allocation policies when keeping (a) current inventory levels and (b) 3 days of inventory.

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