Proceedings of the 2014 Winter Simulation Conference
A. Tolk, S. Y. Diallo, I. O. Ryzhov, L. Yilmaz, S. Buckley, and J. A. Miller, eds.

Modeling the Effect of Shorter Shelf Life of Red Blood Cells on Blood Supplies

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ABSTRACT

In this paper we use simulation to evaluate the effect of shorter red cell shelf life on blood supplies at the Mayo Clinic and compare these results to previous work. Results show that a reduced maximum shelf life of 28 days is supportable under current conditions but that a maximum shelf life of 21 days or less will likely result in unacceptably high outdating rates or unmet patient demand. We also compare the result of discrete event simulation to those of a simple Excel-based simulation and find that the Excel-based simulation predicts a smaller increase in outdating rate in the same scenarios.

1 INTRODUCTION

1.1 Objectives

In the United States unfrozen Red Blood Cells (RBCs) have a maximum shelf life (MSL) of no more than 42 days between removal from a donor and being transfused to a patient. In practice RBCs of all ages are considered equally beneficial to the adult patients receiving them (infants are often given fresher RBCs) However, ongoing research has suggested that fresher blood may result in better patient outcomes, particularly for cardiac and critically ill patients (Koch et al., 2013, Koch et al. 2008, Van de Watering et al. 2006, Aubron et al. 2013). Two large studies (Age of Blood Life Evaluation (ABLE) and Red Cell Storage Duration Study (RECESS)) have been undertaken to resolve the issue but at the time of this paper their conclusions have yet been published. If it is found that fresher RBCs are better for patient health it could potentially lead to reduction of the allowable shelf life, straining already tight RBC inventories.

1.2 Background

A team at Stanford University Medical Center created a small deterministic model (Fontaine et al. 2010) presented in *Transfusion* which evaluated the potential effects of a lowered RBC shelf life on the inventory. They found the potential for RBC shortfall to be as much as 51% and an increase in outdating of up to 3.2% if shelf life was reduced to 7 days.

Mayo Clinic wanted to know what effect a change in shelf life would have on their operations, which differ significantly from the Stanford University Medical Center (SUMC). They also wanted a stochastic model which would capture the uncertainty inherent in the blood supply network where volunteer donors are the foundation and demand is impossible to predict. To know the practical limit of a mandated reduction in age of blood at transfusion would also be valuable. While a reduction to 7 days may be medically beneficial, it may not be feasible from a supply management point of view. The model presented here provided insight into these possible consequences of shelf life reduction and was a valuable tool for Mayo to evaluate other changes to their transfusion operations.

Blood transfusion is a critical part of modern healthcare. According to the Red Cross, more than 40,000 blood transfusions are needed every day in the United States. Facilitating these transfusions is a huge undertaking performed by an interlocking set of local and regional networks with individual donors as the foundation.

Transfusions take place at hospitals which may have their own donor centers or may rely on 3rd parties to provide them with red cells. While the SUMC relies exclusively on Stanford Blood Services, Mayo Clinic has its own donor center and is supplemented with supplies from the Red Cross. In 2010 more than 42,000 units were transfused to almost 9,680 patients at Mayo Clinic. The Mayo Clinic Blood Donor Center delivered 28,772 units to transfusion inventory. Individual hospitals have different ways of managing their RBC inventory, but Mayo is a typical example. At Mayo Clinic patients are given the oldest available RBC with matching type. If matching type is not available compatible units are given. Neonates (infants less than four months old) are the exception to this rule. They are always given blood which is seven days or younger and it is always Rh-negative.

2 STOCHASTIC SIMULATION - MATERIALS AND METHODS

2.1 Why Use Simulation

Because the blood inventory system involves so much uncertainty it was felt that discrete event simulation was the proper tool for a more in-depth study. Additionally, the use of simulation for supply chain management problems has been demonstrated (Chang and Makatsoris 2001). The simulation used in this study was created in Arena 14.0 (Kelton et. al 2002). Random RBC unit arrivals simulated donations to the Mayo Donor Center. The blood type of these units is unknown until their arrival but the processing time and therefore age at receipt is known. An inventory management policy was implemented to drive simulated orders from the Red Cross. The blood type of units arriving from the Red Cross were as ordered but the age of the units varied according to blood type dependent distributions.

2.2 Data

Mayo received 43,455 units into the Transfusion Department in 2010. This includes both units coming directly from the Mayo Donor Center and units ordered from the Red Cross. As seen in Table 1 below, the distribution of units ordered from the Red Cross was similar to the distribution of units donated directly with the exception of AB Positive units, of which only five units were ordered, and O Negative units, which were ordered more than other types, relative to the amount donated directly.

Table 1: 2010 Red Blood Cell Received by Blood Type

Source	A+	A-	B+	B-	AB +	AB-	O+	O-
Internal Donations	34.4%	7.6%	8.8%	1.8%	3.1%	0.6%	35.1%	8.6%
Red Cross	33.1%	7.8%	7.6%	1.1%	0.0%	0.1%	36.9%	13.4%
Total (2010)	34.0%	7.7%	8.4%	1.6%	2.1%	0.4%	35.7%	10.2%

Units coming from the Mayo Donor Center were approximately 3 days old upon receipt with very little variability. However, units from the Red Cross tended to be significantly older and have much greater variability in age at receipt both between and within types (Figure 2). The Red Cross typically sends its newer blood out into the rural areas for transfusion. If unused for a period of time this blood then is returned to the Red Cross and redistributed to the larger hospitals. As one can imagine, this protocol would have a significant impact on future age of blood at transfusion policies.

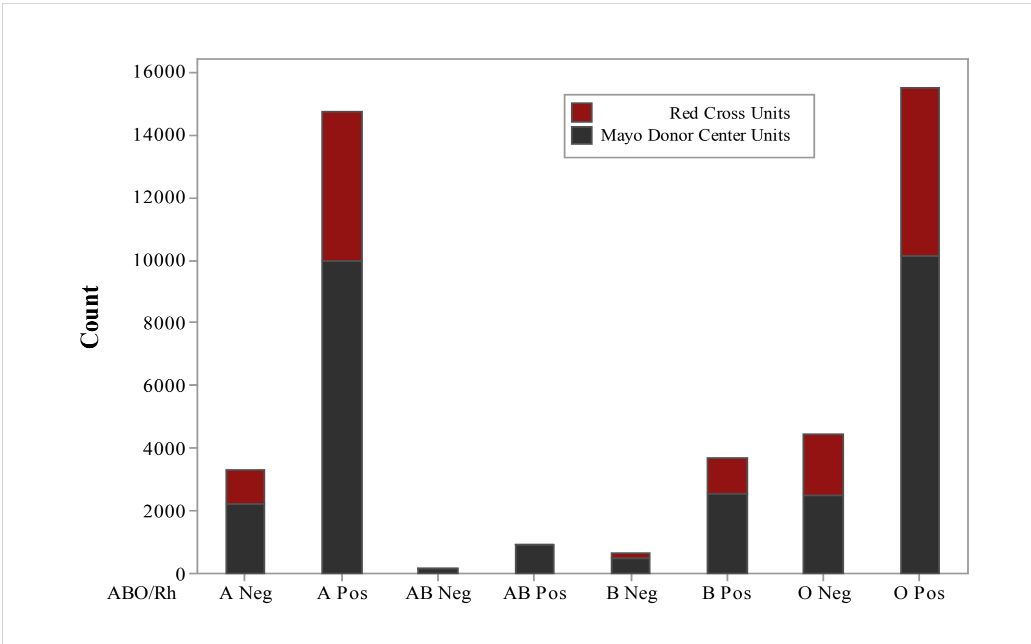

Figure 1: Historical RBC Supply by Source

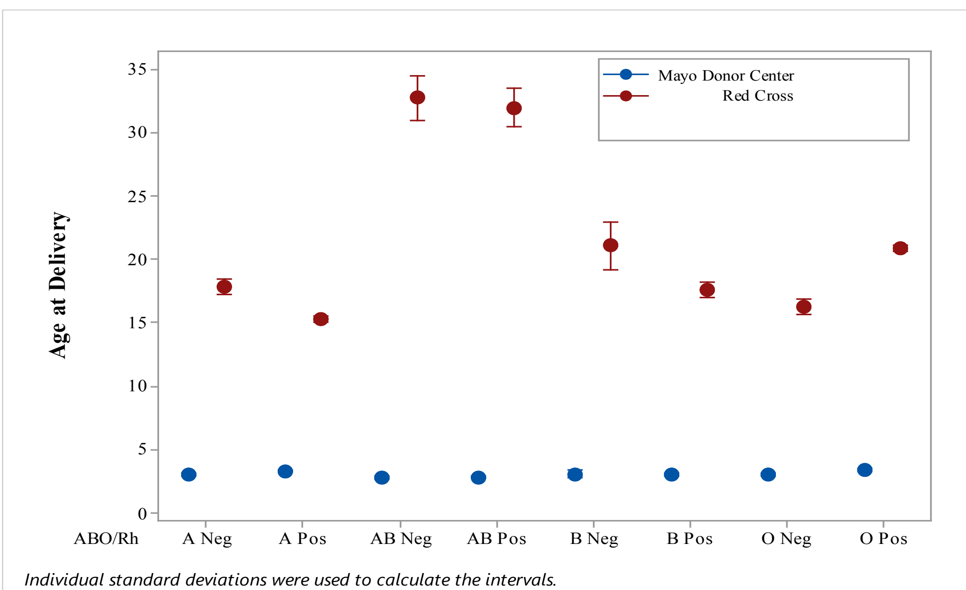

Figure 2: RBC Age at Delivery: Internal Donations vs. Red Cross: 95% CI for the Mean

Under the current policy, the use of Internally donated blood and Red Cross supplied blood has largely been able to maintain direct blood type match demand (Table 4). One of the primary metrics for evaluation of a change in MSL is the number of transfusions which do not match blood type. While some mismatch is acceptable, as noted in Table 2, the desire is to match blood type as much as possible

Table 2: 2010 Adult Patient Data by Blood Type

Patient ABO/Rh	% met by O	% CROSSMATCHED TO SOMETHING BESIDES O	Direct match
A-	8%	4%	88%
A+	7%	3%	90%
AB-	3%	52%	45%
AB+	7%	42%	51%
B-	10%	5%	85%
B+	11%	3%	85%
O-	100%	-	96%
O+	100%	-	94%

An additional important metric is outdated blood. The goal is to waste as little blood as possible while still maintaining a high level of blood transfusion matching. Interestingly the outdating rate for O Negative was higher (5.6%) than the average (4.0%) suggesting that issuing policies tend cause “hoarding” of the valuable O Negative to the point that it outdates before being used. Since O Negative is usable by any blood type it is logical for this blood to be reserved for emergencies. Table 3 shows the outdating rate for the various blood types.

Table 3: RBC Outdating Rate

	A+	A-	B+	B-	AB +	AB-	O+	O-	Total
Outdating Rate	3.7%	3.4%	2.8%	5.0%	2.4%	9.1%	4.4%	5.6%	4.0%

Finally, we are interested in the age of blood at transfusion. This is a dual metric in that part of the modeling looks at how a reduced age of blood at transfusion will affect the system as a whole, we are also interested in the age of blood at transfusion under an acceptable system. Table 4 shows the initial age of blood at transfusion for the different blood types.

Table 4: Historical age of blood at transfusion.

	A+	A-	B+	B-	AB +	AB-	O+	O-
Age of Blood at Transfusion (days)	24.1	29.9	26.6	27.4	15.8	25.8	25.1	24.2

2.3 Simulation Model

We defined six categories of patients based on their medical condition, age and gender (Table 5). Neonates require only O type blood and along with pediatric cardiac patients require RBCs 7 days old or younger in all cases. Women of childbearing age are not allowed to Rh switch (RH positive blood given to an RH negative patient), whereas Rh switching is allowed for other adults. With the exception of pediatric cardiac patients, cardiac patients require RBCs 14 days old or younger only in Scenario 6; discussed below.

Table 5: Patient Category Definition.

Patient Category	Neonate	Pediatric	Women of Childbearing Age	Cardiac	All Others
1	X				
2		X		X	
3			X	X	
4				X	
5			X		
6					X

These patient categories allow realistic approximation of how RBCs are distributed in the hospital (Table 2) and allow for cardiac patients only to be subject to a reduced MSL, as is the case in Scenario 6.

Table 6: Patient Category RBC Requirements.

Patient Category	Type O Only	Blood < 7 days	Can RH Switch	Blood < 14 days (Scenario 6)
1	X	X		
2		X		
3				X
4			X	X
5				
6			X	

Patients were created according to weekday-dependent distributions and assigned a category, blood type and total count of units demanded during the entire hospital stay. These units were transfused across one or more simulated days. This detail was added to capture the impact of correlation of sequential daily demands of specific blood types when a single patient demands blood over several days. After the patient arrived and was assigned attributes, blood inventories were searched for a matching unit of the correct age. If this was not available a compatible unit of desired age was searched. If there was no such unit available other age groups were searched; first for direct matching and then for compatible units.

In the model, RBCs are either generated at the donor center or ordered from the Red Cross. The number of units "received" in the donor center varies randomly by day and the blood types are also randomly assigned. After creation these units are held for two working days of processing time. The Red Cross units are ordered according to the order-up-to inventory policy in place at Mayo at the time the model data was collected. The policy takes into account both what is currently in stock and what is anticipated to arrive from the donor center. The age upon arrival of the Red Cross units is a random distribution (Figure 3) but the types are specified when the units are ordered. Units arrive from the Red Cross the day after they are ordered.

Adult patients arrive randomly by weekday and are assigned blood type, category and number of units demanded. The units will be demanded over one or more days.

Neonate and pediatric entities are representative of units demanded by neonates and pediatrics, to account for the fact that they may receive partial units and that a single regular unit may go to more than one patient. These entities are also assigned blood types.

The simulation attempts to match patient demand with RBCs from inventory. For adults the blood inventory older than seven days was searched for the oldest blood with matching type followed by the oldest available compatible blood. If none is available inventory of units younger than seven days are searched. If there are no compatible units of any age available the patient exits the system. A similar process takes place for neonates and pediatrics except that the oldest blood younger than seven days is considered first and if a match is not found, the youngest blood older than seven days is sought.
The exception to this is in Scenario 6, where (as in the SUMC study) cardiac patients were preferentially given RBCs 14 days old or younger.

2.3.1 The Versions

Seven scenarios were run for each of two models (A and B). Maximum shelf life was the defining characteristic for each scenario, except scenario 6. Scenarios 1-5 were for shelf lives seven, 14, 21, 28 and 35 days respectively (scenarios were limited to seven day increments due to the likelihood of an actual change in MSL policy). Scenario 6 included a seven day limit for blood given to neonates, a 14 day limit for blood given to cardiac patients and a 42 day limit for everyone else. Scenario 7 is the baseline scenario (42 day MSL). In this simulation all scenarios preferred blood seven days or younger for neonates and pediatric patients but in the SUMC study only Scenario 6 contained this feature.

In Model A, if the age of Red Cross units exceeded the MSL of the scenario the age of Red Cross units are lowered to be no more than one day younger than the MSL of each scenario. This was done to ensure that blood received would always have useable life before being aged out, assuming that the Red Cross would follow the same MSL guidelines. In this case if a 14 day old unit was received when a seven day max shelf life was in place, the age of the unit would be reduced to six days. This results in a sort of piling-up of units with age of MSL-1, and leaves limited time to use the unit before it expires.

Model B is representative of a situation where Mayo implements new age limits but the Red Cross does not. Units ordered from the Red Cross have the same age profile for each scenario. For this model in Scenario 1 (MSL of seven days), a 14 day old unit could be shipped to Mayo. However, since the unit is not viable for transfusion it would be immediately rejected. No immediate replacement would be provided. Neither of these treatments of the age of the Red Cross units is particularly realistic, but without knowing how the Red Cross would react to a MSL change, simplifications are necessary.

2.4 Model Verification

Historical Data was input into the simulation model and used to verify and validate the model across several metrics:

- Count of Daily patient arrivals by day of week
- Patient characteristics: category and blood type
- Total units demanded by patients by condition
- % of total units transfused on first day of stay by condition
- Donations to Mayo Donor Center by day of week and blood type
- Age distribution of units received from Red Cross by type
- Quantity of units ordered from Red Cross by blood type

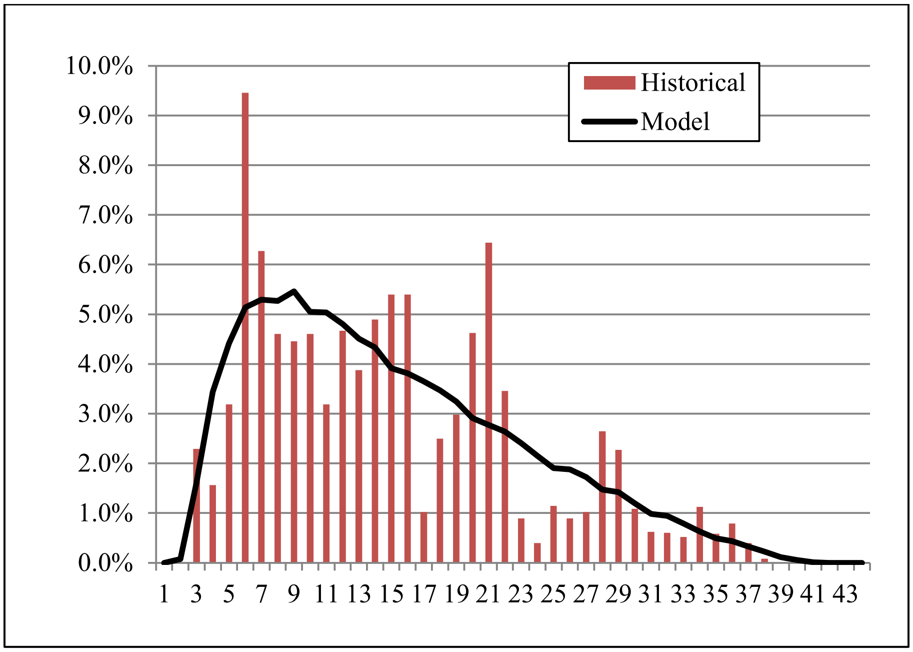

Figure 3: Red Cross Age at Receipt (days) – Historical vs model, A+

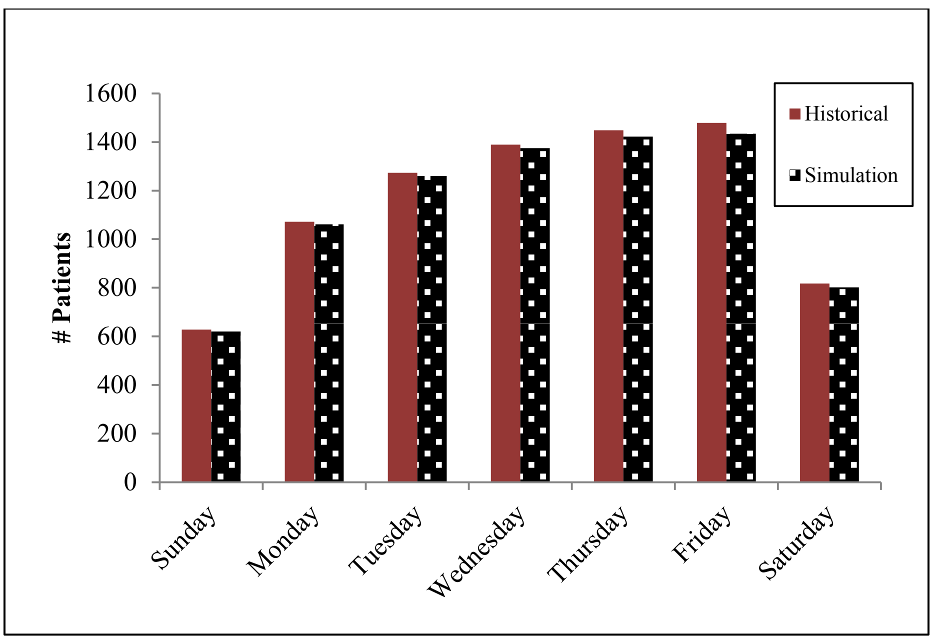

Figure 4: Adult Arrivals by Weekday – Historical vs Simulation

By using the historical internal donation and patient arrivals and demands it was possible to verify the accuracy of the external ordering and the matching portions of the model. In reality the ordering and substitution policies are heuristic rather than absolute so complete agreement between history and simulation is not expected. This is especially true given that a single year's historical data was used.

For all models unless stated otherwise, a warm-up period of 60 days was followed by 10 years of simulation and a cool down period. The cool down period allow collection of outdating data on units in inventory at the end of the 10 year simulation period. Results presented below are the average over all simulated years, excluding warm-up and cool down periods.

3 RESULTS

3.1 Model A

For Model A, where Red Cross units with age at delivery over the MSL are re-aged to be one day younger than MSL, no patient demand went unmet, but it was at the cost of very large number of RBCs outdating. Results are summarized in Table 7.

Table 7: Model A, Red Cross blood modified to follow same policy.

Scenario	MSL (days)	Red Cross Orders		Transfused		Outdated			
		RBCs	Average age at Receipt (days)	Averag e age at Receipt (days)	RBC from RC (%)	Total RBC	RBC outdated (% approx)	RC % of Outdati ng	Overall Average Age at receipt
1	7	76,200	5.79	5.5	95%	63,773	61%	42%	4.5
2	14	54,509	11.05	9.0	83%	42,072	50%	52%	7.2
3	21	22,958	14.48	8.3	49%	10,521	20%	76%	6.3
4	28	13,903	16.25	7.1	33%	1,482	3%	85%	5.5
5	35	12,809	17.14	7.1	31%	387	1%	92%	4.8
6	mixed	12,802	17.27	7.2	31%	384	1%	95%	3.6
7	42	12,581	17.29	7.1	30%	157	0%	98%	3.3

With a seven day MSL, a substantial increase in blood from the Red Cross would be required in order to meet patient needs, the majority of which will outdate before they can be used. In this scenario more than 76,000 units would be requested by Mayo to prepare to meet their patients' needs, 35% of which would eventually be outdated. This is in addition to the nearly 37,000 units from the Mayo Donation center that would outdate. Meeting demand for RBCs with this level of outdating system-wide is not feasible with current rates of donation. The results from this model indicated that a MSL of less than 28 days would likely be infeasible without an increase in blood donations.

3.2 Model B

For Model B (Table 8), where the Mayo Clinic rejects units over their self-imposed MSL, smaller percentages of units shipped to Mayo are acceptable with each lower MSL, as low as 18% when the MSL is 7 days.

Assuming the Red Cross makes no changes to their policies Mayo Clinic would be unable to meet patient demand. Mayo Clinic would reach the capacity for donated blood from the Red Cross. While scenario 1 in Model B is the only replication to result in unmet patient demand, whether the Red Cross would even be able to supply the units at the quantities requested in scenario 1 or 2 is questionable, as the amounts needed would cause a considerable strain on their supply. The unmet demand is a result of rejected units not being instantly replaced. In this scenario demand for 4,039 units went unmet while simultaneously 5,704 units outdated.

System-wide outdating could potentially be less than described in this model because rejected units could conceivably be sent to other hospitals. The overall result for Model B is similar to Model A, 28 days appears to the lowest feasible MSL under current policies.

Table 8: Model B, Red Cross does not make a policy change.

Scenario	MSL	# Units Ordered	# Units Over Age (Drop)	# Units Accepted	% of Request
1	7	76,740	62,686	14,054	18%
2	14	62,249	35,181	27,068	43%
3	21	27,180	9,199	17,980	66%
4	28	16,431	2,512	13,919	85%
5	35	13,377	454	12,924	97%
6	mixed	12,822	9	12,813	100%

Table 9 : Model B Summary

Scenario	MSL (days)	Supply		Transfused		Outdated			Unmet Demand (Units)
		RC Units Accepted	Total	Average Age at Receipt	RBC from RC (%)	Total RBC	% of Total Supply	RC % of Outdating	
1	7	14,054	42,900	3.1	28%	5,704	13.30%	63%	4,039
2	14	27,068	55,914	5.6	54%	14,651	26.20%	32%	0
3	21	17,980	46,827	6.1	40%	5,563	11.90%	27%	0
4	28	13,919	42,765	6.4	33%	1,502	3.50%	31%	0
5	35	12,924	41,770	6.9	31%	507	1.20%	32%	0
6	Mixed	12,813	41,659	7.1	31%	396	1.00%	7%	0
7	42	12,587	41,434	7.1	30%	170	0.40%	8%	0

3.3 Excel Based Simulation

We also created an Excel-based model in the manner described in the SUMC study for comparison to the discrete event simulation models. The Excel model has the same demand as the Arena models but historical units transfused are the only available supply. Compared to the stochastic Arena models the Excel model shows a smaller percent of received units outdating due to fewer units being received. Because additional units are not available unmet demand is significant. Results are summarized in Table 10.

Table 10: Excel Model Summary

Scenario	MSL (days)	RBC Available to be Issued	Decrease in RBC availability	Outdated	Unmet Demand

			Units	%	Units	% of Available	
1	7	29,985	12,009	29%	3,280	8%	15,289
2	14	33,856	8,138	19%	2,510	6%	10,648
3	21	36,994	5,000	12%	1,817	4%	6,817
4	28	39,072	2,922	7%	1,147	3%	4,069
5	35	41,065	929	2%	271	1%	1,200
6	mixed	41,994	0	0%	2,287	5%	2,287

Though the Excel model is incapable of predicting the quantity of incoming RBC units it can be used to set a distant lower bound on the outdating rate.

This model predicts a much smaller decrease in RBC availability than the SUMC Excel model. This can be explained by noting that the average age of units received by SUMC (10.2 days) is higher than the average age of units received by the Mayo Clinic (7.8 days).

3.4 All Models Comparison

Results in previous sections show reasonable outdating rates for Model B and the Excel model (Figure 5). However, this result assumes that rejected units could be used elsewhere and ignore unmet patient demand. The actual effects of a MSL reduction would depend on the reaction of not just the hospitals but also their suppliers such as the Red Cross.

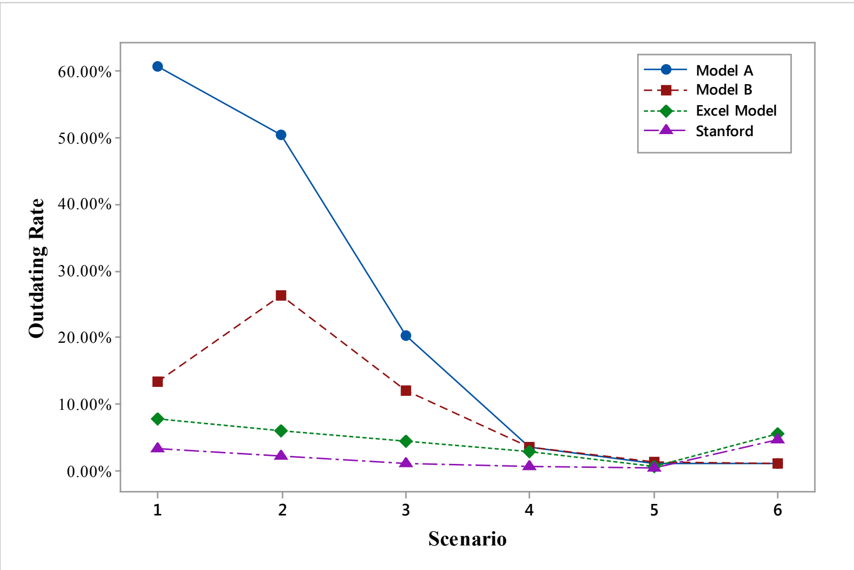

Figure 5: RBC Outdating by Model and Scenario

If the units rejected by a hospital cannot be used elsewhere we must view rejected units as wasted units. Totaling units rejected before being received, as in Model B, with outdating units we can see that the deterministic models are significantly underestimating the quantity of RBCs wasted. As anticipated Models A and B show similarly high rates of RBC wastage; their data in Table 11 suggests that meeting a MSL of 14 days or lower would require a hospital to receive more than double the amount of blood they currently use; an impossible task under the current system.

Table 11: Sum of Unused RBCs and Unmet demand, as Percent of annual demand

Scenario	MSL	Model A		Model B		Excel Model		SUMC	
		Unused RBCs	**Unmet Demand**	**Unused RBCs**	**Unmet Demand**	**Unused RBCs**	**Unmet Demand**	**Unused RBCs**	**Unmet Demand**
1	7	155 %	0 %	166 %	10 %	36 %	36 %	53 %	53 %
2	14	102 %	0 %	121 %	0 %	25 %	25 %	22 %	22 %
3	21	25 %	0 %	36 %	0 %	16 %	16 %	10 %	10 %
4	28	4 %	0 %	10 %	0 %	10 %	10 %	5 %	5 %
5	35	1 %	0 %	2 %	0 %	3 %	3 %	1 %	1 %
6	mixed	1 %	0 %	1 %	0 %	5 %	5 %	5 %	5 %

All models except Model A have restrictions on the quantity of units that can be requested from outside the system. This suggests that if additional units are available, without a change in inventory policy, outdating rates would increase significantly beyond current rates and beyond rates envisioned in other models. All of the models besides Model A also result in unmet demand. We can conclude that there is a tradeoff to be made between service level or outdating rates and reduced MSL. Without changes to the system that allow fresher blood to be delivered a MSL of 7 days would not allow patient demand to be met. It would appear that 28 days is the lowest feasible sustainable MSL. However, without knowing more about how the blood supply network would react it is impossible to say more specifically what outdating rate or unmet demand would be.

4 CONCLUSION

Our simulations illustrated the tradeoff between outdating rates and unmet demand. Like the SUMC study we suggest that 28 days is the lowest MSL feasible under the current system. Using the Excel model as comparison to the SUMC study demonstrates that the impact of a reduced MSL will vary depending on a hospital's patient population and RBC supply. We find that the Excel model underestimates outdating and gives no information on increased inventory needed. The stochastic models allowed us to estimate the range of increase in supply that would be needed.

There are some limitations regarding understanding the external behavior of the Red Cross to a change in MSL. Our models assume that the required blood would mostly be delivered so long as the requested amounts did not exceed the overall limits to requests. However, if all institutions moved towards the same reduction in MSL the more likely result would be an inability to meet system demand. So while it may eventually prove to be beneficial to provide younger blood to patients, the ability to substantially reduce the MSL may be impractical or impossible to achieve under current blood donation levels.

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