Factors affecting red blood cell storage age at the time of transfusion

Walter H. Dzik, Neil Beckman, Michael F. Murphy, Meghan Delaney, Peter Flanagan, Mark Fung, Marc Germain, Richard L. Haspel, Miguel Lozano, Ronald Sacher, Zbigniew Szczepiorkowski, and Silvano Wendel

BACKGROUND: Clinical trials are investigating the potential benefit resulting from a reduced maximum storage interval for red blood cells (RBCs). The key drivers that determine RBC age at the time of issue vary among individual hospitals. Although progressive reduction in the maximum storage period of RBCs would be expected to result in smaller hospital inventories and reduced blood availability, the magnitude of the effect is unknown.

STUDY DESIGN AND METHODS: Data on current hospital blood inventories were collected from 11 hospitals and three blood centers in five nations. A general predictive model for the age of RBCs at the time of issue was developed based on considerations of demand for RBCs in the hospital.

RESULTS: Age of RBCs at issue is sensitive to the following factors: ABO group, storage age at the time of receipt by the hospital, the restock interval, inventory reserve, mean demand, and variation in demand.

CONCLUSIONS: A simple model, based on hospital demand, may serve as the basis for examining factors affecting the storage age of RBCs in hospital inventories. The model suggests that the age of RBCs at the time of their issue to the patient depends on factors external to the hospital transfusion service. Any substantial change in the expiration date of stored RBCs will need to address the broad variation in demand for RBCs while attempting to balance considerations of availability and blood wastage.

Whether or not red blood cells (RBCs) that have been stored under refrigerated conditions adequately deliver oxygen to tissues or result in adverse consequences for transfusion recipients is a topic of intense current scrutiny. Dozens of studies registered at clinicaltrials.gov, including four large multicenter randomized controlled trials, are investigating the potential for RBCs with a reduced storage age to improve clinical outcomes. Policy decisions regarding the current expiration date for RBC should await the results of these clinical trials. Regardless of their outcome, any substantial reduction to the current RBC expiration period might be expected to decrease blood inventories and to increase blood outdating.[1] However, the magnitude of the effect on blood availability and wastage remains uncertain. Previous studies have sought to model the balance between availability and outdating especially as applied to platelets (PLTs), which have a short shelf life.[2-4]

From the Massachusetts General Hospital, Boston, Massachusetts; Filton Blood Centre, Bristol, UK; John Radcliffe Hospital, National Blood Service, Oxford, UK; University of Washington, Seattle, Washington; New Zealand Blood Service, Auckland, New Zealand; Fletcher Allen Health Care, Burlington, Vermont; Hema Quebec, Ste-Foy, Quebec, Canada; Beth Israel Deaconess Medical Center, Boston, Massachusetts; Hospital Clinic Provincial, Barcelona, Spain; Hoxworth Blood Center, Cincinnati, Ohio; Sírio Libanês Hospital, São Paulo, Brazil; and Dartmouth-Hitchcock Medical Center, Lebanon, NH.

[Correction added after online publication 03-Apr-2013: Affiliations have been updated.]

Address correspondence to: Walter H. Dzik, Blood Transfusion Service, Massachusetts General Hospital, Room J-224, 55 Fruit Street, Boston, MA 02114; e-mail: sdzik@partners.org.

From the Biomedical Excellence for Safer Transfusion Collaborative: http://www.bestcollaborative.org/.

Received for publication November 14, 2012; revision received January 7, 2013, and accepted January 7, 2013.

doi: 10.1111/trf.12171

TRANSFUSION 2013;53:3110-3119.

Recently, Belien[5] provided a thorough review of the published literature on the supply chain of blood components. The author reviewed nearly 100 publications that have used a variety of methods to address blood supply chain management, including best practices, simulations, queuing models, stochastic dynamic programming, integer programming, linear programming, statistical analysis, cost analysis, what-if scenario analysis, and custom spreadsheets. Nagurney and colleagues[6-8] have further advanced the analysis by focusing on network analysis of blood as a perishable item. However, nearly all published work has focused on models developed from the perspective of supply by blood centers, and almost no studies have specifically addressed a general model for the effects of reducing RBC storage intervals.[5]

In this article, members of the Biomedical Excellence for Safer Transfusion (BEST) give a general presentation of the key factors, based on considerations of demand, that determine the age of RBCs at the time of issue; illustrate these factors with real-world examples drawn from six nations; and offer a framework by which to quantify the relationship between blood wastage and availability as a function of blood storage age. We anticipate that this approach can be applied to larger data sets and will prove to be of value to decision-makers wishing to better understand the consequences of a reduced RBC storage interval.

MATERIALS AND METHODS

Spreadsheets were produced for collating information on RBC inventories from hospitals and blood centers. The spreadsheets included a section for the collection of basic information on the hospital or blood center and separate sheets for the daily collection of data on RBC inventory, issue, and discards.

The following data were collected from hospitals: number of beds, type of facility, distance from the supplying blood center, and time taken for routine deliveries to arrive; local policy for RBC shelf life, mean number of crossmatches per RBC, mean time between crossmatch and issue, mean number of RBCs issued per day, number of routine deliveries each week, number of ad hoc deliveries each day, and whether the hospital receives RBC from other depots; policies for crossmatch by age of RBCs, discard by age of RBCs, the mean number of units issued each day, target levels of inventory, and levels that trigger inventory restocking; methods for calculation of inventory level and the software used for control of blood inventory. The data collection exercise for hospitals recorded the above data by individual ABO group. We separately recorded inventory levels according to storage age by ABO and Rh group for routine, irradiated, and phenotyped RBC inventories. The data collection exercise was run for a 1-week period at each participating hospital. Participating hospitals were from the United States, Brazil, England, New Zealand, and Spain. Blood centers provided data on the age of RBCs in inventory according to ABO and Rh group. Participating blood centers were from the United States, Canada, and New Zealand.

Inventory data were used to define the impact of a reduced RBC shelf life based on current hospital practice. The percentage of inventory, by blood group, greater than an age of 7, 14, 21, 28, and 35 days was assessed. The inventory replenishment practice and target stocks were used to calculate a suite of RBC inventory management measures by blood group. These included target for the number of days stock, percentage of target stock in inventory, percentage of stock used each day, reorder level as a percentage of target inventory (action limit), and reorder level defined as days of inventory remaining.

RESULTS

Baseline characteristics of 11 BEST member hospitals who supplied inventory data are shown in Table 1. Hospitals ranged in size from 341 to 902 beds and maintained daily total RBC inventories that ranged from 167 to 767 units. Table 2 shows measures describing the RBC inventory at participating hospitals. Table 3 shows the proportion of the RBCs in stock according to storage age, and Table 4 shows the distribution of storage age of RBCs at the time of issue.

Reduced RBC expiration affects hospital inventories first

Not surprisingly, the age distribution of RBCs is offset toward a longer storage age in hospitals compared with blood centers. Figure 1 shows representative data for group O RBCs from three blood centers and from the 11 participating hospitals. Because a reduction in storage age would more adversely affect hospital inventories than blood center inventories, the rest of this analysis will focus on drivers of hospital inventory. However, as shown in Fig. 1, an extremely reduced RBC expiration date would affect inventories in blood centers as well.[1] As shown in Fig. 1, the percentage of group O RBCs in hospitals that expire before transfusion under the current 42-day expiration date is low. For example, at Hospital I in our survey, the percentages of RBCs among each ABO and Rh group that expired in 2012 were as follows: O+, 0.1%; O–, 0.2%; A+, 0.1%; A–, 0.3%; B+, 0.1%; B–, 0.7%; AB+, 6.6%; and AB–, 5.4%.

Volume of RBCs in hospital inventories

Three factors drive the volume of RBCs maintained in hospital inventories: 1) mean number of RBCs transfused per restock period, 2) the variance on the volume transfused

TABLE 1. Baseline characteristics of BEST member hospitals submitting inventory data (n = 11)

Characteristics	Hospital										
	A	B	C	D	E	F	G	H	I	J	K
Bed size	341	850	750	400	650	631	360	466	902	500	350
Nation	Brazil	England	Spain	New Zealand	New Zealand	US	US	US	US	US	US
Deliveries per week	n.r.	17	10	4	5	5	5	7	2	3	4
Trauma unit (yes/no)	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Distance from blood center (km)	<5	<5	5-10	>50	<5	25-50	25-50	<5	25-50	<5	<5
Mean number of RBC units in inventory	174	170	416	189	317	587	167	233	767	233	154*
Mean number of RBC units presumed transfused per day	20	63	98	11	34	50	24	49	102	22	25
Inventory management policy	FIFO	FIFO	FIFO	FIFO	FIFO	FIFO LIFO†	FIFO	FIFO	FIFO	FIFO	FIFO

* Data for Group O+ and O− only.
† LIFO for AB− only.
FIFO = first in, first out; LIFO = last in, first out; n.r. = not recorded.

per restock period, and 3) the "reserve" needed for unexpected demands. The mean demand for RBCs is a function of clinical activity and will vary depending on hospital size and services offered. A small community hospital that does not support trauma services, cardiac surgery, or major orthopedic surgery will have a very different demand than a large hospital supporting transplantation, cardiac surgery, and trauma. The variance surrounding mean demand is also a key factor affecting the size of the inventory required. Hospitals with wide variation in demand will require a larger inventory than hospitals with highly consistent demand, all other factors being equal. For example, a small hospital with episodic responsibility for trauma care will require sufficient inventory to support occasional episodes of massive transfusion. In reality, the variance surrounding demand can be substantial. For example, at Hospital I in our survey (902 beds in the United States) the mean demand for O+ RBCs during a 2-month period was 36 units per day with a standard deviation (SD) of 16 units.

Blood reserve is the third factor affecting blood volume in inventory. For supply chain models where the consequences of running out of stock are not dire, inventory reserve is not an essential driver. However, in other circumstances, such as the national supply of oil, strategic reserve is critical. Because the consequences of running out of blood for transfusion are dire, reserve is an essential driver of hospital inventory decisions. Because the variance in demand is a measure of episodes of high-volume usage, the level of reserve can be quantified by a factor we term "R" (Reserve) which is multiplier of the SD of mean demand.

$$\text{Inventory volume} = \text{Restock interval in days} \times [\text{Mean daily demand} + (R \times SD_{\text{mean demand}})]. \quad (1)$$

For example, setting $R = 2$ would imply a sufficient volume of RBCs in inventory to cover two SDs (approx. 95%) of RBC demand during restock intervals—a level that most hospitals would find very inadequate because, for a facility restocked daily, there would be an insufficient supply of blood on average every 40 days. Setting $R = 6$ would be more akin to "Six Sigma" management. Actual levels are likely to be between these extremes. For example, because Hospital I has a mean daily inventory for O+ RBCs of 202 units, a restocking interval of every 2 days, a mean daily demand of 36 O+ units, and a SD of demand of 16 units per day, then for O+ RBCs at this hospital: $202 = 2 \times [36 + (R \times 16)]$ and $R = 4.1$.

ABO and reserve

The value for inventory reserve (R) is different for different ABO groups. Because group A recipients can receive group O RBCs, hospitals can draw on both A and O stock

TABLE 2. Inventory and replacement measures at 11 hospitals based on data collected during 1 week

Measure	Hospital: / Hospital bed number:	A 341	B 850	C 750	D 400	E 650	F 631	G 360	H 466	I 902	J 500	K 350
Proportion of inventory turnover per day												
O+		0.07	0.56	0.27	0.08	0.12	0.12	0.18	0.24	0.19	0.12	0.09
O–		0.07	0.20	0.13	0.04	0.07	0.06	0.09	0.19	0.10	0.07	0.10
A+		0.22	0.60	0.27	0.06	0.13	0.07	0.15	0.20	0.15	0.13	n.r.
A–		0.11	0.15	0.17	0.08	0.08	0.05	0.14	0.14	0.06	0.13	n.r.
Reorder level: proportion of optimal stock level triggering reorder												
O+		0.51	0.33	0.48	0.69	0.59	0.47	0.48	0.50	0.75	0.50	0.65
O–		0.54	0.33	0.60	0.56	0.74	0.62	0.23	0.54	0.57	0.50	0.83
A+		0.51	0.38	0.48	0.73	0.64	0.47	0.42	0.56	0.63	0.50	0.65
A–		0.55	0.27	0.50	0.67	0.60	0.63	0.43	0.59	0.75	0.60	1.00
Stock fulfillment: proportion of target stock in inventory												
O+		1.12	1.11	0.80	0.98	1.35	0.88	0.94	0.66	1.15	1.30	1.20
O–		0.42	1.00	0.90	1.04	1.23	1.51	1.27	0.93	1.19	1.67	1.13
A+		0.33	1.00	0.80	0.96	1.26	0.76	1.13	0.87	1.00	0.90	n.r.
A–		0.81	1.33	0.88	0.87	1.04	2.00	1.00	1.71	1.93	0.80	n.r.
Optimal reserve (days): target level/mean transfused per day												
O+		13.6	1.6	4.6	13.0	6.1	9.5	5.8	6.3	4.5	6.5	9.8
O–		35.0	5.0	8.3	27.0	11.7	10.8	8.7	5.6	8.8	9.0	8.8
A+		13.8	1.7	4.6	18.3	6.4	19.0	6.0	5.6	6.7	8.3	15.2
A–		11.0	5.0	6.7	15.0	12.5	10.0	7.0	4.3	8.0	9.8	11.1
Minimum reserve (days): reorder level/mean transfused per day												
O+		6.9	0.5	2.2	9.0	3.6	4.5	2.8	3.1	3.4	3.2	6.4
O–		19.0	1.7	5.0	15.0	8.7	6.7	2.0	3.0	5.0	4.5	7.4
A+		7.0	0.6	2.2	13.3	4.1	9.0	2.5	3.2	4.2	4.1	9.8
A–		6.0	1.3	3.3	10.0	7.5	6.3	3.0	2.5	6.0	5.9	11.1

TABLE 3. The proportion of RBCs *in inventory* greater than the specified age

Storage age (days)	Hospital: / Hospital bed number:	A 341	B 850	C 750	D 400	E 650	F 631	G 360	H 466	I 902	J 500	K 350
O+												
7		0.80	1.00	0.91	0.94	0.95	0.99	0.21	0.20	0.65	0.99	0.75
14		0.38	0.90	0.53	0.58	0.39	0.49	0.00	0.03	0.25	0.84	0.02
21		0.01	0.30	0.11	0.13	0.03	0.14	0.00	0.02	0.08	0.39	0.02
28		0.00	0.11	0.00	0.00	0.00	0.06	0.00	0.02	0.03	0.05	0.01
35		0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.01	0.00	0.00	0.01
O–												
7		0.28	1.00	0.86	0.90	0.97	0.98	0.75	0.42	0.86	0.99	0.60
14		0.16	0.99	0.61	0.72	0.64	0.78	0.46	0.20	0.60	0.87	0.00
21		0.00	0.79	0.25	0.38	0.47	0.51	0.39	0.19	0.32	0.62	0.00
28		0.00	0.55	0.01	0.10	0.25	0.26	0.20	0.18	0.09	0.34	0.00
35		0.00	0.00	0.00	0.00	0.00	0.11	0.02	0.08	0.02	0.08	0.00
A+												
7		0.27	1.00	0.88	0.99	0.96	1.00	0.93	0.85	0.67	0.99	0.99
14		0.05	0.99	0.33	0.73	0.66	0.42	0.24	0.25	0.26	0.88	0.87
21		0.00	0.59	0.04	0.28	0.11	0.22	0.03	0.04	0.10	0.53	0.63
28		0.00	0.14	0.02	0.00	0.03	0.07	0.00	0.04	0.00	0.15	0.20
35		0.00	0.00	0.01	0.00	0.00	0.02	0.00	0.03	0.00	0.01	0.01
A–												
7		0.08	1.00	0.79	0.86	0.99	0.98	0.80	0.99	0.83	0.99	0.88
14		0.04	1.00	0.27	0.32	0.48	0.79	0.22	0.66	0.47	0.84	0.01
21		0.04	0.92	0.04	0.03	0.11	0.42	0.12	0.35	0.22	0.63	0.00
28		0.04	0.34	0.00	0.01	0.00	0.18	0.02	0.05	0.05	0.28	0.00
35		0.00	0.00	0.00	0.00	0.00	0.06	0.00	0.01	0.00	0.08	0.00

to support episodes of high demand. However, because only group O RBCs can be used for group O recipients, hospitals must maintain a higher reserve of group O compared with group A, all other factors being equal. Because group O– recipients with anti-D can only receive group O– RBCs, it would be expected that group O– RBCs would be kept at highest reserve relative to their actual demand. Maintaining a larger reserve supply in inventory is expected to cause the mean shelf life of that product to be longer. This was observed in our hospital survey data. As seen in Table 4, for each hospital the proportion of older RBCs (21 or 28 days of storage) was always higher for O– units compared with O+ units. Similar results were seen for A– compared with A+. The

TABLE 4. The proportion of RBCs *issued* greater than the specified age

	Hospital:	A	B	C	D	E	F	G	H	I	J	K
Storage age (days)	Hospital bed number:	341	850	750	400	650	631	360	466	902	500	350
O+												
7		1.00	1.00	1.00	0.98	1.00	1.00	0.49	0.64	0.58	1.00	n.r.
14		0.82	0.92	0.91	0.52	0.94	0.65	0.08	0.09	0.13	1.00	n.r.
21		0.14	0.32	0.55	0.43	0.17	0.12	0.08	0.09	0.02	0.67	n.r.
28		0.09	0.10	0.06	0.05	0.05	0.05	0.04	0.04	0.02	0.33	n.r.
35		0	0	0.03	0	0	0.02	0.04	0.03	0.01	0.22	n.r.
O–												
7		0	1.00	0.98	0.75	0.68	1.00	1.00	0.63	1.00	1.00	n.r.
14		0	0.92	0.91	0.63	0.53	1.00	0.56	0.45	0.84	1.00	n.r.
21		0	0.66	0.77	0.46	0.37	0.93	0.44	0.38	0.61	1.00	n.r.
28		0	0.35	0.11	0.38	0.05	0.78	0.44	0.30	0.33	0	n.r.
35		0	0	0.11	0	0	0.59	0	0.23	0.08	0	n.r.
A+												
7		0.55	1.00	0.97	1.00	0.99	1.00	1.00	0.94	0.73	1.00	n.r.
14		0.18	1.00	0.84	0.85	0.89	0.61	0.82	0.62	0.25	1.00	n.r.
21		0	0.54	0.04	0.71	0.52	0.45	0.18	0.17	0.17	1.00	n.r.
28		0	0.11	0	0	0.20	0.23	0.09	0.15	0.01	0	n.r.
35		0	0	0	0	0	0.09	0.09	0.11	0	0	n.r.
A–												
7		0.25	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	n.r.
14		0.25	1.00	0.85	0.60	1.00	1.00	1.00	0.95	0.84	1.00	n.r.
21		0.25	1.00	0.10	0.20	1.00	0.71	0.67	0.86	0.57	1.00	n.r.
28		0.25	0.38	0	0.20	0	0.46	0	0.14	0.37	1.00	n.r.
35		0	0	0	0	0	0.38	0	0	0	1.00	n.r.

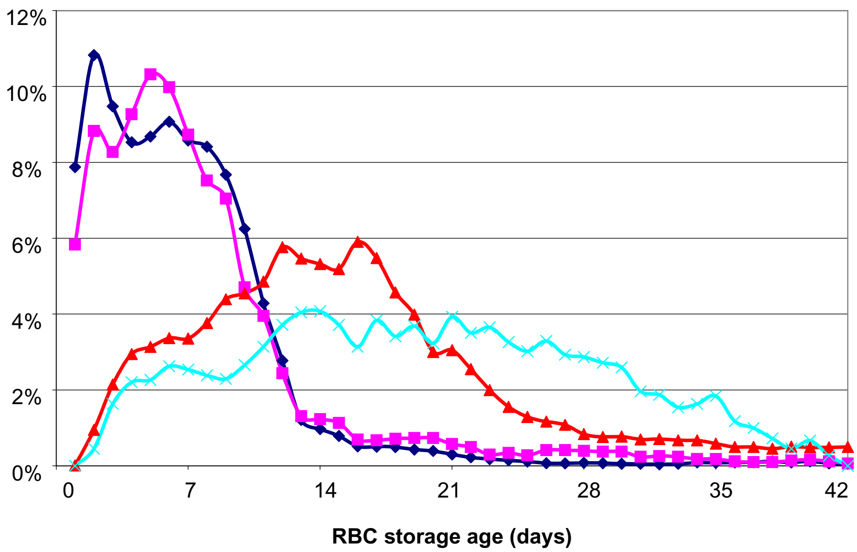

Fig. 1. Distribution of group O RBCs according to storage age. The percentage of RBCs in inventory is shown, averaged for three blood centers and eleven hospitals. The mean age of RBCs is greater for hospitals than blood centers, the distribution of age is broader for hospitals than blood centers, and the age is greater for O D– than D+. See text for details. (◆) O+ (blood center); (■) O– (blood center); (▲) O+ (hospital); (×) O– (hospital).

findings are in agreement with those recently published by Sayers and Centilli.[1]

Hospital RBC inventory turnover

Supply chain theory underscores that inventories with high turnover have a shorter shelf life. Thus the proportion of inventory turnover will affect the mean age of RBCs in hospital inventories. Daily turnover can be expressed as a simple proportion of the volume of inventory distributed, as:

$$\text{Mean daily turnover} = \frac{\text{Mean number of RBC units transfused per day}}{\text{Number of RBC units in inventory}}. \quad (2)$$

Consistent demand versus episodic demand will affect the observed turnover, all other factors kept equal. As extreme examples, consider two hospitals each of which distributes 50 RBCs per day. One hospital is a specialty cancer hospital distributing 50 ± 10 RBC units per day and restocked daily. If R = 3, then the volume in inventory is $1 \times [50 + (3 \times 10)] = 80$ RBC units and the mean daily turnover is 50 of 80 or 62%. In contrast, a community hospital with responsibility for episodic motor vehicle trauma distributes 50 ± 30 RBC units (larger variation) and the restock interval is every 4 days (more distant from blood supplier). If R = 3, then the volume in inventory is $4 \times [50 + (3 \times 30)] = 560$ and the mean daily turnover is 50 of 560 or 9%. Thus, inventory turnover and its associated effects on RBC storage age might be expected to vary widely among hospitals depending on their individual circumstances. This was observed in the data obtained from the BEST member hospitals surveyed. As shown in Table 2, the proportion of the group O+ inventory that turned over each day varied more than eightfold among the different hospitals. Hospital B (850 beds in England) is restocked with RBCs every 12 hours and thus can maintain a smaller inventory. As a result, Hospital B has a 56% turnover rate for O+ RBCs and a 60% turnover rate of A+ RBCs. In contrast, Hospital D (400 beds in New Zealand) is restocked four times per week and maintains an inventory of 189 units with a daily turnover of only 8% for group O+ and 6% for A+ RBCs.

Regardless of policy for inventory management, inventory turnover is directly related to the mean shelf life of RBCs. The smaller the proportional turnover of stock, the longer RBCs "sit on the shelf" awaiting distribution. The minimum mean age of RBCs at the time of issue is related to the reciprocal of daily inventory turnover, as

$$\text{Minimum mean RBC age} \rightarrow \frac{1}{\text{Mean daily turnover}}. \quad (3)$$

Thus, all other factors being equal, hospitals with a high daily proportion of inventory turnover will have a reduced age of RBCs at the time of distribution. However, other factors, as described below, affect the age of RBCs at the time of issue. This was shown in our data where 32% of RBCs at Hospital B were issued at more than 21 days of storage despite this hospital having the highest daily inventory turnover.

Variance in turnover affects hospital RBC storage age at time of issue

Because the proportion of inventory turnover is not constant, the age of RBCs in inventory will vary over time. For example, during a period of consecutive days when demand is below average, the proportion of inventory that is turned over will decrease below its average and RBCs will remain in inventory resulting in a slight increase in mean RBC age at the time of issue. During periods of high demand on consecutive days, the opposite effect occurs. At Hospital I the mean daily turnover of group O+ RBCs was 0.19 with a SD of 0.1. Accounting for the variance in turnover adds an additional factor to the expected RBC age in inventory as

$$\begin{aligned}\begin{matrix}\text{Minimum age}\\ \text{at issue}\end{matrix} &= \begin{matrix}\text{Mean age when}\\ \text{received}\end{matrix} + \begin{matrix}\text{Time to place}\\ \text{into inventory}\end{matrix}\\ &+ \frac{1}{\text{Mean daily turnover}} + \lambda \times SD_{\text{mean turnover}}.\end{aligned} \quad (4)$$

The value of λ accounts for the time required for turnover to return to the mean. The value assigned to λ depends on one's tolerance for RBC wastage due to outdating. A larger value for λ will result in less outdating, but will allow a longer RBC storage age in inventory.

Combined effects of drivers on the minimum expected RBC storage age

The combined effects of the above drivers can be used to estimate the minimum expected RBC age at the time of issue, as

$$\begin{aligned}\begin{matrix}\text{Minimum age}\\ \text{at issue}\end{matrix} &= \begin{matrix}\text{Mean age when}\\ \text{received}\end{matrix} + \begin{matrix}\text{Time to place}\\ \text{into inventory}\end{matrix}\\ &+ \frac{\begin{matrix}\{\text{Restock interval}\\ \times[\text{Mean daily demand} + (R \times SD_{\text{demand}})]\}\end{matrix}}{\text{Mean daily demand}} + \lambda \times SD_{\text{turnover}}.\end{aligned} \quad (5)$$

where R reflects the value placed on inventory reserve and λ reflects the value placed on avoidance of wastage by outdating.

As an example, data from Hospital I, a large urban hospital with trauma, cardiovascular surgery, and transplantation services demonstrate that even with perfect inventory management, the mean age of O+ RBCs can currently be no less than 16 days at the time of issue as shown in Table 5.

DISCUSSION

Recent clinical interest has focused on the age of RBCs at the time of transfusion. RBC storage age depends on the overall blood supply chain and the efforts to balance supply and demand for a perishable product.[5,9-11] Most previous studies have focused on the blood distribution perspective in supply chain management with considerations for optimal efficiency, availability, and minimal RBC wastage. These models were developed assuming the current expiration date for RBCs and did not focus on the impact of a substantial reduction in expiration date.[5]

Recently, Fontaine and coworkers[12] examined the potential effect on blood inventories resulting from a

TABLE 5. Example of estimating the minimum mean age of RBCs at the time of issue based on input factors*

Input of supply and demand data	
Mean storage age at time of receipt of RBCs from blood supplier (days)	10
Mean number of days to place RBCs in service at hospital (days)	1
Restock interval (days)	2
Mean number of units transfused per day (units)	36
SD of the mean number of units transfused per day (units)	16
SD of the mean percentage of turnover of inventory (expressed as a proportion)	0.1
Input of value judgments	
R is the multiplier of SD of mean number transfused units per day	4.1
λ is the multiplier of the SD of mean inventory turnover	2
Outputs	
Mean number of units transfused per restock period (units)	72
Mean volume in inventory required (units)	203.2
Mean daily inventory turnover (as a proportion)	0.177
Mean *minimum* age of RBCs issued (days)	16.8

* The input data are real data for group O RBCs from Hospital I. The outputs are determined by Eq. (5) shown in the text.

reduction in RBC expiration date. They used inventory data from the Stanford University Medical Center and the Stanford Blood Center to model the effect of a reduced RBC expiration date on availability and outdating of RBCs. They observed that RBCs were received with a mean age of 10.2 days and remained on the shelf for a mean of 8.6 days with a mean age at distribution of 18.8 days. While their model failed to consider the adjustments in supply or restock intervals that would accompany a change in expiration date, they reported that a reduction in maximum shelf life from 35 days to 7 days would be predicted to result in a 50% decrease in the number of available units and a fourfold increase in the number of units outdated per year. They noted that their model was restricted to data generated from one hospital and did not represent a generalized model for the effect of reduced RBC expiration on blood availability and outdating.

We provide an initial consideration of some of the drivers that affect the minimum possible age of RBCs distributed by hospitals. Our analysis neither assumes that the current expiration date for RBCs should be sustained nor promotes the adoption of a shorter RBC shelf life. Although first in, first out is the most commonly used inventory management policy for blood stocks, our analysis does not depend on any particular inventory management policy. Our analysis assumes ideal inventory management based on observed demand and thus predicts the *minimum* achievable RBC storage age for any specific set of input variables. In reality, other factors also influence blood inventory levels and thus the storage age at the time of transfusion. As reviewed by Stanger and coworkers,[13] these include experience in inventory management, transparency, use of electronic crossmatching, and collaborative values between the hospital laboratory and clinical staff regarding blood utilization and wastage. We would add other factors that include the level of advanced life support technology of the hospital (ability to sustain a critically ill patient), health care reimbursement systems, adoption of new surgical procedures that may result in massive blood loss, clinical trends in trauma care, and cultural issues surrounding prolonged and aggressive life support in critical care units.

The importance of an adequate reserve of available blood

Blood inventory management focuses on an optimization that minimizes blood wastage as a result of outdating while preserving an adequate reserve inventory for blood availability.[3] Most practitioners do not assign equal weight to these two issues and consider an adequate reserve supply to be of paramount importance. Nevertheless, excessive outdating is economically wasteful and would be expected to create a substantial disincentive to blood donors. Custer and colleagues[14] included the cost of replacing wasted units in their supply chain model for a regional blood center. The relative values assigned to reserve and wastage (represented by R and λ in Eq. [5]) are very important drivers of any policy regarding the RBC expiration date. The age of blood at issue is likely to be more sensitive to changes in R than λ. For example, if a hypothetical hospital receives a restock shipment every 4 days consisting of RBCs with a mean age of 7 days, requires 1 day to bring the RBCs into available inventory, and transfuses a mean of 50 ± 25 units per day (200 ± 100 per restock interval) with a SD of inventory turnover of 0.2, and if λ is fixed at 2.0, then as R varies from 2 to 10, the minimum required volume of RBCs in stock will vary from 400 to 1200 units and the mean age of RBCs at the time of issue will vary from a minimum of 10.4 days to a minimum of 14.4 days. If R is fixed at 6, then as λ varies from 2 to 10, the volume of RBCs in stock will not change but the minimum mean age at issue will vary from 12.4 to 14 days.

Demand versus restocking

The number of units transfused per unit of time (the flux of RBCs) is directly driven by demand for transfusion. However, hospital inventories are not replenished in a continuous minute-to-minute basis. While blood is issued in real time, restocking is episodic and several factors specific to restocking will affect the volume of RBCs that the hospital seeks to maintain as reflected in the R reserve. These factors include but are not limited to distance from blood supplier to hospital, reliability of transport, interruptions due to weather, blood center performance in

TABLE 6. Possible effects of progressive reduction in RBC shelf life on the blood supply*

RBC shelf life (days)	Blood center/supplier	Large urban hospital located near supplier	Small community hospital located far from supplier
35	Minimal increase in collections (<1%).	Minimal effects.	Minimal effects.
28	Reduced flexibility for redistribution of RBCs.	Wastage increase.	Wastage increase.
	Increased frequency of distribution to remote hospitals.	Reduced flexibility for return and redistribution.	Reduced flexibility for return and redistribution.
	Moderate increase in collections.	More frequent deliveries.	More frequent deliveries.
21	Markedly reduced redistribution flexibility.	Increased wastage.	Wastage substantially increases due to reduced second wave of distribution.
	Shift stock away from B, AB toward use of A, O. Change in the donor base.	Move from B and AB to increased O, A.	Move from B and AB to increased use of O, A.
	Marked increase in collections.	Increased use of D+ RBCs for nonsensitized D– recipients.	Increased use of D+ RBCs for nonsensitized D– recipients.
	Increased marketing and publicity.	Increase in emergency deliveries.	Increase in emergency deliveries.
14	Decentralize to establish more collection and distribution centers. Donation to processing times prevent the manufacture of some components (using current standards).	High daily inventory turnover.	Increased turnover.
	Very limited redistribution.	Reliance on group O for B and group A for AB recipients.	Only group A or O available.
	Substantial increase in collections.	Increased use of D+ for D– recipients.	Increased use of D+ for D– recipients.
	Consider increased donation frequency, reduced donation volumes (250 mL), and donor iron supplementation.	Wastage rates very high.	Wastage rates very high.
	Greater reliance on automated RBC collections (e.g., double donations) with concomitant decrease in whole blood–derived PLTs.	RBCs held in local storage depots awaiting results. Local labeling and release.	Inadequate blood available for trauma, GI bleeds on more frequent occasions.
	Establish emergency contingency stock with longer shelf life or frozen RBC contingency.	Just-in-time delivery. High number of small deliveries.	Just-in-time delivery. High number of small deliveries over extended distance.
	More and smaller TTD testing centers colocated at storage depots or hospitals.	Contingency supply of “expired” O– or O+ RBCs held in central location.	Contingency supply of “expired” O– or O+ RBCs held in central location.
	Increased proportion of “split” RBC components. Increased donor exposure.	Clinical requests for RBCs not filled based on strict adherence to guidelines.	Clinical requests for RBCs not filled based on strict adherence to guidelines.
7	Storage on roving distribution vehicles only.	Inadequate blood available for major surgery, trauma, cardiac, and cancer care.	Inadequate RBC availability for most nonroutine patient needs.
	Consider reduction in donation interval or reduced donation Hb limits.	Some testing, labeling, component manipulation, or release performed at hospitals if distant from supplier.	RBCs not discarded at outdate
	Limited RBC storage at blood center. Common use of contingency stock due to shortages (e.g., frozen RBCs or “expired” RBCs >7 days old).	Surgery rescheduling each day based on RBC availability.	Contingency RBCs (“expired”) routinely used.

* Possible effects on blood suppliers and hospitals are shown for weekly decrements in RBC shelf life. Progressive reduction in RBC storage would likely result in increasing pressure for a single “vein-to-vein” integrated information system for all hospitals that share blood supply, significant reduction of centralized inventory and distribution system, and comprehensive contingency arrangements including agreed upon mechanisms for use of RBCs beyond expiration date.

meeting delivery expectations, pricing policies, penalties for return of unused stock, hospital policies that accept "short-date" (older) units from blood centers, hospital laboratory staffing, ABO group, and the time required to move units from received status to available status. We suggest that hospital restock interval be used as the "unit of time" when calculating mean demand. In general, the longer the restock interval, the greater the mean RBC storage age will be at the time of issue.

Consistency of demand

Consistency of demand, represented by the SD of daily use or the SD of inventory turnover, plays an important role in the final RBC storage age at the moment of transfusion. Supplemental orders from blood suppliers cannot be used to support actively bleeding patients because demand is urgent and because existing hospital transfusion staff members are occupied with direct support of the patient. Supplemental orders are useful for restocking after the immediate crisis has ended. Thus, hospitals with a large variance in demand require larger in house inventories and thus tend to transfuse RBCs with a greater storage age. Variation in demand is not under the control of blood services and can be affected by numerous events such as the introduction of new programs in transplantation or trauma, recruitment of surgeons who specialize in high-risk procedures, or changes in patient referral patterns resulting from large practice shifts such as hospital mergers or from seemingly small and unrelated events such as changes to patterns of ambulance triage in major cities.

Possible effects on the blood supply resulting from reduced RBC expiration date

Our approach allows a first glimpse at possible consequences of a progressive reduction in the expiration date for RBCs. A summary of possible effects is shown in Table 6 and represents expert opinion based on data, but not proven evidence. The description assumes a single RBC expiration date for all transfusion recipients. The wisdom behind the selective application of fresh RBCs to one recipient group has been questioned.[15] Any policy in which a substantial proportion of hospital transfusions are restricted to fresh blood for selected patient groups would be expected to shift the mean storage age of RBCs to units older than current practice for those patients not restricted to fresh transfusions. Because the supply chain is interdependent, a progressive reduction in RBC shelf life would have impact on both blood suppliers and hospitals. All negative effects would be more pronounced in settings where the delivery time between blood supplier and hospital is prolonged. A reduction in RBC expiration from 42 days to 35 days would be expected to have little impact on patient care or RBC wastage. In the absence of changes to hospital restocking, an expiration date of 28 days would be expected to result in increased outdating of O–, AB, and B RBCs with the need to increase donor recruitment of O– donors to maintain current reserves in inventory. A reduction in the expiration date to 21 days would be expected to require widespread changes to blood distribution policies and restock intervals with substantial increases in collections and a shift toward the use of group A RBCs for AB recipients and group O RBCs for group B recipients, thereby eliminating stocks of AB and B RBCs, which would otherwise expire awaiting transfusion. We project that an expiration date of 14 days would have substantial negative impact on hospital reserves and would require a substantial increase in national collections to preserve hospital inventory volumes. Despite such efforts, an inadequate supply of RBCs would be expected to occur in situations of high demand. For major surgical procedures and trauma, policies that triage RBCs among different patients and place limits on massive transfusion would likely be required. An expiration date of 7 days for RBCs would be expected to result in a profound disruption of the national blood supply.

Our work is subject to an important limitation. While the data collected represent examples that illustrate the current status of hospital blood inventories, we recognize that data from a very much larger group of hospitals will be needed to validate the general application of the principles outlined. Also our data did not include seasonal variations that can affect the blood supply.

In summary, we provide a general approach for estimating the minimum mean age of RBCs at the time of issue to the patient. Key drivers of the age of RBCs at the time of issue include ABO group, storage age at the time of receipt by the hospital, the restock interval, need for inventory reserve, mean demand, and variation in demand. The latter three factors are not in the control of the hospital transfusion service and are likely to vary substantially among different hospitals in developed nations of the world. Consideration of "demand factors" outside the control of blood services will be essential to any policies regarding RBC expiration date. Blood inventory management will continue to depend on a complex task of meeting demand while balancing availability and wastage across a varied health care landscape.

CONFLICT OF INTEREST

None.

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