Platelet pool inventory management: theory meets practice

Wim de Kort, Michiel Janssen, Nikky Kortbeek, Naud Jansen, Jan van der Wal, and Nico van Dijk

BACKGROUND: The shelf life of platelet concentrates (PCs) is a matter of days. Simultaneously, the demand is highly variable, shortages are not allowed, and producing too many results in outdating. Concurrently, younger PCs, implying an extended time till outdating (TTO), are preferred. Common PC inventory management relies on experience-based order-up-to rules. This study aimed at minimizing outdating and shortages, while extending the TTO through a theoretical approach. It focuses on PCs processed from whole blood donations.

STUDY DESIGN AND METHODS: A combined approach of stochastic dynamic programming and simulation techniques (SDP/S), from the mathematical discipline operations research, has been implemented. This approach included the design of the dedicated software tool thrombocyte inventory management optimizer (TIMO). Based on the 2007 data, an optimal order-up-to rule was calculated. Outdating percentages and TTOs have been collected from August 2005 to July 2010. The resulting order-up-to rule has been applied and adjusted from summer 2007 onward.

RESULTS: Over the study period, the results of the practical implementation showed significant improvements. The median weekly outdating percentage dropped to less than 1% and a gain in TTO of 0.48 day was reached. The results and the additional computer simulations brought confidence to the personnel to apply and adopt the "theoretical" approach and TIMO.

CONCLUSION: Applying theory may help a blood bank to improve its PC inventory management and may help to identify to what extent practical limits can approach theoretical limits. The application of the theory has led to both a significant improvement and a more structured and less panic-driven PC inventory management.

One of the most fragile products of the blood bank is the platelet concentrate (PC). The production process and storage conditions of PCs require precision and the shelf life is a matter of days. Simultaneously, production and inventory management of PCs must meet a highly variable demand, while shortages are not allowed: selling "no" is not an option, because a life may be at stake. Although with quite some effort the demand at hospitals is partially foreseeable, the larger proportion of the demand that blood banks are faced with remains highly uncertain. In addition, imminent shortages require extra efforts from the staff, taking time, extra costs, and giving rise to stress to both the blood bank and the hospitals. In contrast, producing too many PCs results in spill due to outdating. This gives rise to a waste of production costs and, as the supply of blood relies on donors who donate at a voluntary, nonremunerated basis, outdating is also undesirable for ethical reasons.

Older studies for blood banks and hospitals in Western Europe and the United States report that 15% to 20% of the produced platelet (PLT) pools are disposed due to outdating. A more recent study concerning the efficiency of blood PLT production in 10 European countries mentions an average outdating figure of 14%.[1] In blood management literature, in contrast, various simulation

ABBREVIATIONS: PC(s) = platelet concentrate(s); SDP/S = stochastic dynamic programming and simulation; TIMO = thrombocyte inventory management optimizer; TTO = time till outdating.

From Sanquin Blood Supply, Nijmegen; and the Department of Operations Research, University of Amsterdam, Amsterdam, the Netherlands.

Address reprint requests to: Wim de Kort, Sanquin Blood Supply, Geert Grooteplein Zuid 34, 6525 GA Nijmegen, the Netherlands; e-mail: w.dekort@sanquin.nl.

This study and the development of TIMO was financially supported by Sanquin Blood Supply and the University of Amsterdam, without the pursuit of profit.

Received for publication December 24, 2010; revision received March 9, 2011, and accepted March 18, 2011.

doi: 10.1111/j.1537-2995.2011.03190.x

TRANSFUSION 2011;51:2295-2303.

studies have been reported,[2-7] but without formal support or structural approaches.

Blood bank practice

In blood banks all over the world PC inventory management often relies on a production rule known as an order-up-to or replenishment rule. For each day of the week this rule prescribes the number of PCs to be produced to be equal to a preset level: no more, no less. The prevailing order-up-to rules are purely empirical and at best suboptimal, giving rise to the outdating percentages mentioned above. Moreover, nobody has a clue on what other than empirical grounds these order-up-to levels are set. Being not based on "hard" calculations, these rules are often handled less strictly, leading to ad hoc, sometimes even panic-driven, adjustments through purchasing or extra production. Subsequently, inventory levels vary even more so than demand levels do, leading to both exaggerated shortages and outdating. This was also the case in the Sanquin Blood Bank Southeast Region, despite a shelf life extension of PCs to 7 days. A more structural approach was warranted.

New approach: stochastic dynamic programming and simulation

In a previous article,[8] a theoretical framework was presented on tackling this inventory management problem. The paper showed that, theoretically, a substantial decrease of outdating and shortages could be attained. The theoretical framework is based on the combination of two methods: stochastic dynamic programming (SDP) and simulation (S), known from the mathematical discipline of operations research. Operations research is the discipline that studies transport, queuing, and inventory problems by mathematical modeling. More precisely for the PC inventory problem:

- SDP is used to compute and establish an optimal production policy, and
- simulation is used to conclude to a practical rule from the optimal production policy.

From hereafter this combined new approach will be referred to as SDP/S. The result of SDP/S is an order-up-to rule. In former research, theoretical results of SDP/S, as based on 1-year historical data, appeared most promising.[8] However, until now, no practical real-life implementation and improvements had taken place. On the outset, in blood transfusion environments—both blood banks and hospitals—order-up-to rules are common practice. Such rules are known to be "optimal" in standard inventory theory for nonperishable products. However, for perishable products, such as the PC, their value is not known.

Early dynamic programming formulations for blood inventory problems can already be found in the 1970s in operations research literature.[9-12] However, with the exception of recent work,[13] no numerical results have been reported due to computational complications and limitations. As a first step of the current practical SDP/S implementation study the numerical procedures and simulation, as developed by Van Dijk and coworkers,[8] have been integrated in a software tool called thrombocyte inventory management optimizer (TIMO).

Age of PCs

A feature of PC inventory management not explicitly dealt with in the article by Van Dijk and coworkers is the current preference to administer PCs of only a few days, that is, 1 to 3 days old as opposed to PCs of an older age, that is, 4 to 6 days,[8] as during shelf life changes in PCs take place, including activation and some deterioration,[14,15] which some may consider to be detrimental. Moreover, some hospitals prefer an in-hospital inventory of PCs. To this end, hospitals request products that are as young as possible. Therefore, age is an additional, independent property of PCs that deserves separate attention. The complementary feature of age, the time remaining until the PC unit outdates—referred to as time till outdating (TTO)—contains the same information, but must be interpreted in combination with the accepted shelf life.

This article deals with both aspects, outdating and age (TTO) of PCs in a blood bank, simultaneously holding risk on shortage very low. More specifically, it aims to study the effects within a real-life blood bank environment of

- the SDP/S approach and
- the SDP/S implementation through TIMO.

To this end, a comparison is made between the results of desktop calculations through SDP/S and the practical results of empirical PC inventory management, where desktop results have been implemented. For an understanding of the results, first a brief description is presented on the PC production, release, and issue process in the Sanquin Blood Bank Southeast Region.

PC PRODUCTION PROCESS AT THE SANQUIN BLOOD BANK SOUTHEAST REGION

The Sanquin Blood Bank Southeast Region collects blood and plasma in the southeastern part of the Netherlands. Altogether this regional blood bank collects per annum approximately 150,000 whole blood donations and 90,000 apheresis donations, predominantly plasmapheresis donations. They supply 28 hospitals with blood products: per annum approximately 145,000 red blood cell (RBC) units, 20,000 units of plasma for transfusion, and 11,000 PCs. Approximately 98% of the PCs supplied are produced by the buffy coat method (pools of five); the

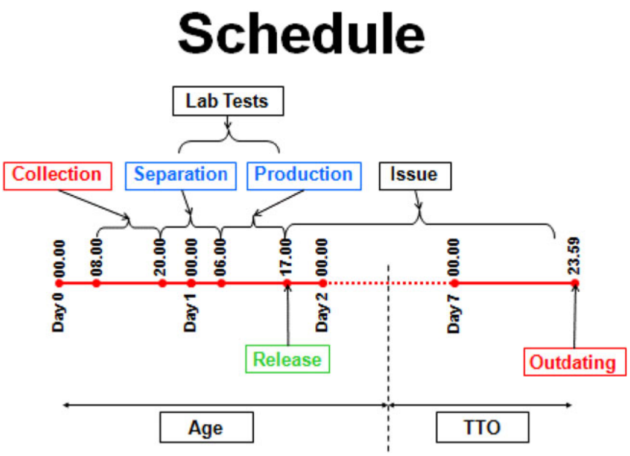

Fig. 1. Time schedule for the production, release, and issue of PCs.

remainder are single-donor apheresis PCs, including HLA/HPA-matched PCs and small- and low-volume PCs for the newborn.

At Day 0 between 8:00 AM and 8:00 PM, whole blood collections take place at one of the 35 blood donation locations of the Sanquin Blood Bank Southeast Region (see Fig. 1).

The donations are brought to the production location in Nijmegen. Directly after arrival the production process starts: the separation of the whole blood donation into units of RBCs and plasma and a buffy coat. Buffy coats of five donations, together with the plasma unit from one of these five donations, are pooled and fractionated into a PC and stored at 20 to 24°C. In parallel with the production process, various bacterial and quality tests are performed. The age of blood products is measured in days. For comparison reasons, the age of all blood products are set at 1:00 on 0:00 AM on Day 1. Note that the actual time elapsed since the donation of the concerned blood products at that moment is in fact less than 1.0: between 0.17 and 0.67 days. At 8:00 AM on Day 1 the decision with respect to the amount of pools to produce is made and the actual production process of PCs starts. The production and testing is finished at 5:00 PM on Day 1 and the PCs are released for issue at that time point. So, the regular issue of PLT pools can effectively start in the evening of Day 1, the minimum age of a PC being 1.7 days. The PCs are issued to one of the 28 hospitals in the region, seven of which do keep a permanent minor inventory themselves of one to seven PCs. Pools become outdated (expire) at 12:00 PM on Day 7. Therefore, the maximum time from releasing till outdating is 6.3 days, leaving effectively 6 days for PCs to be issued. The minimum time elapsed from the collection time onward to the time of expiration is 7.3 days, the maximum time being 7.7 days.

Empirical PC inventory management at the Sanquin Blood Bank Southeast Region

After centralizing the three (sub)regional production facilities into one facility located in Nijmegen, the Netherlands, in June of the year 2005, the production department started to adjust its order-up-to rule for PC production on an empirical basis in the year 2006. In 2007 and 2008 a thorough evaluation on production, outdating, and shortages took place and a comparison was made with SDP/S results to further optimize the order-up-to rule: see the results section for quantitative data. To this end a software tool (TIMO) has been developed (University of Amsterdam), which enabled the production department to periodically calculate and adjust its order-up-to rule, when the trend in the demand suggested this. In the appendix (available as supporting information in the online version of this paper) a brief description of TIMO is presented. TIMO is formally in use as of November 2008 at the Sanquin Blood Bank Southeast. Ahead of this formal introduction, experience-based narrowing down of the order-up-to rule and stricter compliance with the order-up-to rule started in the summer of 2007 already. During and after the period of introducing TIMO the Sanquin Blood Bank Northeast Region was standby for supplying extra PCs in case of shortages.

MATERIALS AND METHODS

Theoretical modeling: SDP/S approach

The SDP/S approach combines two operations research techniques: stochastic dynamic programming and computer simulation. Dynamic programming is a mathematical optimization technique to efficiently solve multiple decision problems in which periodically decisions must be taken such as decisions on which direction you go to find a shortest route in a network. SDP is its extension in which uncertainties (stochastics) are also to be taken into account.[16,17] This is clearly the case for PC production because the demand is highly stochastic. (For an instructive illustration of DP and a brief discussion on its PC inventory application see the link mentioned in Appendix S1 of the electronic version of the Van Dijk article.[8]) Computer simulation is a technique to mimic a process of interest—here the PC inventory evolution—over a long period of time, for example, one or several years, in just a fraction of time, for example, a few minutes. The technical, mathematical, computational, and numerical details of this combination of steps have been reported earlier.[8,18] Basically, SDP computes an optimal production decision for each day and possible inventory state x. Here, x describes the PC inventory state on a particular day of the week in terms of both the number of PCs and their age. Subsequently, while taking into account all possible demand uncertainties and all possible production levels, optimal production decision rules can be computed for each day of the week. Here, optimal means that the production decisions computed come with the lowest possible average costs. These costs directly reflect outdating and shortages. However, when applying the SDP technique to the PC inventory problem two complications appear.

- Due to the size of the state space (the number of possible states x), the required computer memory and the number of computations (in the order of 10^{50}) are prohibitively large for realistic computation. An intermediate simplification of the problem is required, for example, by downsizing through formation of aggregates.
- The "optimal policy" is far more complex than just a simple order-up-to rule. However, the simple order-up-to rule is a good and practical approximation.

The SDP/S-based approach integrates, in a five-step regime, the mathematical SDP computations with simulation to provide a nearly optimal (i.e., within 2% optimality) simple order-up-to rule. This rule prescribes an order-up-to (production) level for each day of the week, independent of the actual inventory state x. Briefly, the five essential steps can be summarized as follows.

Step 1 (*SDP formulation*): An SDP formulation is given with fictitious costs for outdating and shortages. The ratio between these two cost components determines the "importance" of both events.

Step 2 (*downsizing and computation*): This SDP problem is reduced in size by aggregating the demand units (pools) to multiples of (for example) 5, as to make a numerical approach possible.

Step 3 (*simulation frequency table*): The optimal policy is evaluated by means of simulation. The structure of the optimal strategy is displayed in order-up-to decision frequency tables.

Step 4 (*simple rule detection and optimality test*): From these tables one or more simple order-up-to rules are distilled (the most frequent ones) and evaluated by simulation, comparing its results with those of the optimal policy computed in Step 2.

Step 5 (*simulation optimality test and resizing*): After resizing (from units of 5 back to units of 1), the simple order-up-to rules are (re)evaluated by simulation, resulting in one rule to be applied in practice.

TIMO

In former research,[8] these steps have been executed "theoretically" using 1-year historical data. For its practical implementation, as part of the present research, these steps have been integrated in a software tool called TIMO. Blood bank employees themselves could directly apply TIMO without having to understand theory or having to execute each step separately. In addition to the five SDP/S steps, TIMO has two additional features:

- (*Learning by simulation*) The software tool was also applicable to simulate any given order-up-to rule that can be practically used or different levels that one might use. By this step blood bank practitioners could "test" the rules in use *objectively* as well as *compare* different order-up-to rules (levels) against the "optimal" ones as computed by Steps 1 through 5.
- (*Age/TTO*) One could include "penalty costs" for older PCs, for example, PCs older than 5 days and again study and simulate its impact.

Theoretical analysis

The theoretical analysis was applied in three steps.

Actual 2007 data

First, from the blood bank information system, data of the year 2007 were extracted on the number of PCs issued per week, the outdating percentages, and the number of PCs bought from other blood bank regions. At the start of the year 2007 the production order-up-to rule varied from 90 to 105 on Mondays to 120 to 140 on Fridays and another 20 PCs on Saturdays. This variation in the rule was prompted more by the daily variation in stock than by the variation in demand from the hospitals.

Base case (using the actual 2007 data)

Then, using the data on the number of PCs issued per week in the year 2007, a base SDP/S was performed to calculate theoretical achievable data on shortage, outdating, and mean age at the time of issue. In agreement with reality, 5 production days (Tuesday through Saturday) were used, where Saturday's production limit was 20 units. The results were compared with the actual results of the year 2007.

Modified theoretical case

Some adjustments in the production scheme in the Sanquin Blood Bank Southeast production scheme were modeled to see if further improvement could (theoretically) be reached. A focus was placed on adjustments in the production capacity.

Analysis of actual data: outdating percentages, TTO

Of all PCs issued between August 1, 2005, and July 31, 2010, weekly outdating percentages were calculated and plotted. In addition, the TTO was calculated by assessing the time in hours between the time of issue and outdating time of that PC. TTO of outdated PCs was set at zero. The TTOs of 1 week were averaged and this average TTO was plotted against the calendar weeks. For statistical analysis the 5-year period was divided into five periods (Year 1 to Year 5), each year starting in August of the respective year.

The third period (from August 2007 to August 2008) was the period when TIMO has been developed and first adaptations of the order-up-to rule have been made. Average results of TTO and outdating percentages were calculated for every year.

Differences were statistically assessed using either t test in case of normally distributed data (the average weekly TTO) or the Mann-Whitney U test in case of skewed data (the average weekly Out%). If applicable, univariate regression lines were calculated by a statistical software package (EViews 5, IHS, Inc., Irvine, CA), where we applied the Newey-West correction for robust standard errors. All other statistical tests were performed with statistical software (SPSS 17, SPSS, Inc., Chicago, IL).

RESULTS

In line with that described under Materials and Methods, we first describe the theoretical analysis consisting of 1) the actual 2007 data on which the theoretical analysis is applied, 2) the theoretical results of the SDP/S approach on the base case, and 3) the theoretical results of the SDP/S approach on the production capacity extension case. The practical results in the full study period are then presented. Finally a short account is given on the issue of acceptance by the employees.

Theoretical SDP/S modeling results on the actual 2007 data

Actual 2007 data

The number of PCs produced in 2007 was 11,331, including 150 units (1.3%) bought from other regions at 5 different days throughout the year (1.4% in days, in every case a Monday or a Tuesday). Cases of buying units from other regions were defined as cases of shortage. Losses due to nonoutdating reasons, such as a positive screening test result, or production losses involved 381 units, leaving 10,950 PCs free for delivery. In fact, 10,527 PCs, that is, 202 PCs per week have been delivered. With 423 units being outdated, the outdating percentage in 2007 was 423/10,950 = 3.9%. Notably, a considerable part of the outdating did not take place at the blood bank. Of the 423 units produced and released, in fact 157 units (=1.4%) outdated at the blood bank. At the hospitals from their inventory 266 units (=2.4%) outdated by local, largely unknown inventory management mechanisms. Based on a detailed tracking data during 8 weeks (Weeks 21-28 in 2007), the mean daily demand on Monday through Friday was 36 with a standard deviation (SD) of 10, while on weekend days this mean was 12 (SD 8).

Base case (using the 2007 data)

With the 2007 data we could model the production and its order-up-to levels of PCs with several assumptions using TIMO. In this first study only two cost elements are used, outdating and shortage costs. Shortage costs are taken to be five times as high as the outdating costs, which is considered to be a best guess and includes extra working time to produce the necessary number of PCs. The issue policy is on a first-in–first-out or FIFO basis (that is, the oldest compatible PCs are issued first). The results are displayed in Table 1, which gives the order-up-to rule with the levels for Monday through Sunday, the performance with respect to shortages and outdating as a fraction of the annual demand, and the mean age and the age distribution of the issued PCs (the distribution starts with the percentage of PCs issued at shelf age 1 day and then the percentage for age 2 days, etc.). The asterisk in 162* in the order-up-to rule for Saturday indicates that the order-up-to level is 162 but, in practice, there is a limited production capacity of 20 PCs in this case. This notation is also used in Table 2.

Despite the aforementioned, substantially larger demand variance for the present case, as opposed to the case reported by Van Dijk and coworkers,[8] theoretical shortage and outdating percentages are still excellent. The SDP/S approach is highly robust for demand variation. Note that the order-up-to levels for Tuesday through Thursday are very similar. The order-up-to level for Friday is considerably higher, 165, because of the limited production capacity on Saturday and the production stops on Sunday and Monday. Compared to the 2007 performance mentioned earlier, with an outdating level of 1.4%, these order-up-to levels in theory could give a very considerable improvement. Also shortages could be almost nonexistent: SDP/S calculates a shortage of approximately four PCs per year, occurring on one occasion. In contrast, the issue age of the PCs still remains fairly high, with a mean age of 3.75 days, implying a theoretically achievable TTO of 4.25 days.

TABLE 1. Theoretical SDP/S of the base case (2007 data)

Factor	Theoretical results	Actual 2007 data
Replenishment rule (Monday-Sunday)	(0; 131; 131; 134; 165; 162*; 0)	(0; 90-105; 95-105; 105-123;120-140; 20; 0)
Shortage	0.04% (approx. four pools per year)	1.4% (150 units on 5 days)†
Outdating	0.25% (approx. 25 pools per year)	1.4% (157 units)‡
Mean age/TTO (days)	3.75/4.25	4.4/3.6

* Theoretical order-up-to level. On Saturdays in practice, as a rule, 20 PCs have been produced.
† On five different occasions the blood bank decided to buy 30 units from other blood bank regions.
‡ A total of 1.4% (157 units) outdated at the blood bank, and an extra 2.4% (266 units) outdated in the hospitals. See text for further explanation.

Modified theoretical case

To see if further improvement in TTO values could be attained through Step 6, SDP/S calculations were performed, increasing the production capacity on Saturday to 40 and to add a limited production of an extra 20 PCs through apheresis on Monday morning, together with an extra screening test run the same day. The results are shown in Table 2. It shows with such a production scheme a theoretically achievable issue age of 3.6 days, implying a TTO of 4.4 days.

Practical results in the full study period: outdating percentages and TTO

Figure 2 shows a graph of the PC Out% per week over the same 5-year period. The coefficient of –0.018 outdated PCs per week implies a predicted drop from 4.66% PCs outdated per week at the starting point to only 0.1% at the blood bank at the end of Year 5.

TABLE 2. Theoretical SDP/S results of the base case (2007 data), build out with a production capacity increase on Saturday to 40 units and adding an extra production of PCs through apheresis on Monday morning

Replenishment rule (Monday-Sunday)	(132*; 129; 129; 131; 153; 147*; 0)
Shortage	0.02% (approx. two pools per year)
Outdating	0.06% (approx. six pools per year)
Mean age/TTO (days)	3.6/4.4

* Theoretical order-up-to levels. On Mondays, production capacity is limited to 20 PCs, collected through apheresis; on Saturdays, 40 PCs are produced.

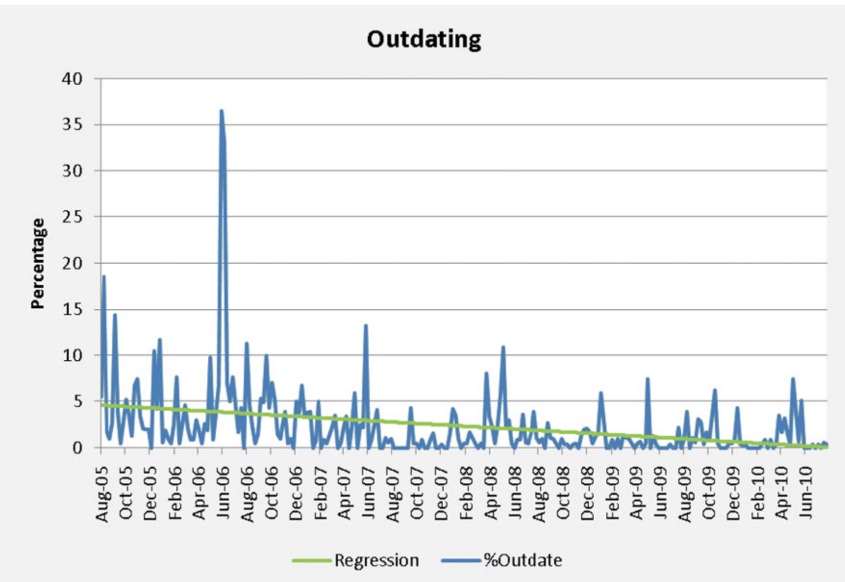

Fig. 2. Weekly actual percentage of outdated PCs set against the calendar time as of August 2005. The line equation is (standard errors in parentheses): Out% = 4.662 (0.86)% – 0.018 (0.005)% × Number of weeks elapsed since August 2005.

In addition, Fig. 3 shows a graph of the weekly mean TTO against time. The coefficient of +0.0019 days per week implies a predicted gain in TTO of 0.50 days over a time period of 5 years from 3.31 days at baseline to 3.81 days at the end of Year 5.

The Out% and TTO statistics are summarized in Table 3. The data show a significant decrease in Out% in Year 3, the starting point of working with calculated order-up-to levels. The data also show that a substantial increase in TTO already became visible in Year 2, the starting point of implementing empirical order-up-to levels. A significant improvement in mean TTO was reached in Year 5. Clearly, the improvement in outdating is somewhat more prominent due to the fact that the SDP/S (TIMO) approach optimizes to costs directly related to outdating. In addition, shortages—again defined as situations where PCs have been bought from other regions—occurred two times in both the year 2008 and the year 2009, while in the first half-year of 2010 no shortages occurred, as opposed to five instances of shortage in the year 2007.

Practical acceptance and smoothing

Based on both the results themselves and the ability of "learning by simulation," a general acceptance has been developed to "trust" and use prescribed order-up-to levels as computed by SDP/S (TIMO) and not to react overly panic, such as on Monday mornings. Only minor adjustments, supported by simulation were made. Accordingly, the combined "theoretical-practical" approach has led to a far more structured and "relaxed" PC inventory management, with improved results, as reported earlier.

DISCUSSION

The University of Amsterdam and Blood Bank Nijmegen have developed the user friendly software tool TIMO, based on operations research methods, after the first theoretical SDP/S exercise, performed in the Sanquin Blood Bank Northeast Region. It was obvious that a substantial reduction in outdating of PCs would be achievable. The empirical adjustments of the order-up-to production rules in the Sanquin Blood Bank Southeast Region—started in 2006—already brought along a great improvement. With the help of SDP/S calculations a further reduction in outdating of blood bank stored PCs and an extension of the TTO was reached: The introduction of TIMO in Year 3 brought the mean TTO up from 3.52 days in Year 2 to 3.64 days in Year 3. This TTO gradually grew to 3.73 days in Year 5, a significant improvement compared to both Year 1 and Year 2. The 5-year period TTO increase involves 0.48 days. Since most PCs are issued once a day, this mean increase in TTO at the time of issue of 0.48 days (12 hr) means that one in every two PCs issued in Year 5 has a TTO increase of 1 full day, compared to PCs issued in Year 1.

Given the current production capacity, the theoretical mean TTO within reach was 4.0 days with very low numbers of outdating and shortages. An additional production capacity increase (20 PCs on Saturday) resulted in a theoretical TTO within reach of 4.25 days. Thus, the practical TTO level in Year 5 (3.73 days) differed only 0.52 days from the current theoretical TTO level. Hand in hand with the gradual increase in TTO, a gradual decrease in the Out% at the blood bank has come up. Year 3, the TIMO introductory year, brought a significant decrease in Out% that could be kept constant through to Year 5: in the Years 3 to 5 the weekly Out% showed a median of 0.5%, as opposed to 2.8% in Year 1 and 2.2% in Year 2. It must be borne in mind that some of the assumptions in the SDP/S model deviate from practice and, vice versa, some practical circumstances are not part of the model.

First, in the region, there are three distribution points instead of one. This is the consequence of the agreement with hospitals that in emergency situations, a blood product such as a PC, once issued, must be at the hospital within 1 hour. With only one distribution point several hospitals in the region could not be served within 1 hour.

Second, in-hospital outdating is relatively high for several reasons. For hospitals with a local inventory, this inventory management is complicated, because their inventory levels are fairly low. In addition, the number of PCs used in some of those hospitals does not justify the use of a local inventory of PCs and facilities for conditioned storage are lacking. In nonconditioned situations, a PC outdates at 6 hours after the time of issue. The outdating of PCs, once issued from the blood bank or the local inventory, is complicated further due to changing patient conditions. Regularly, the change in the patient's situation makes the physician abandon or postpone the transfusion with a subsequent outdating being imminent.

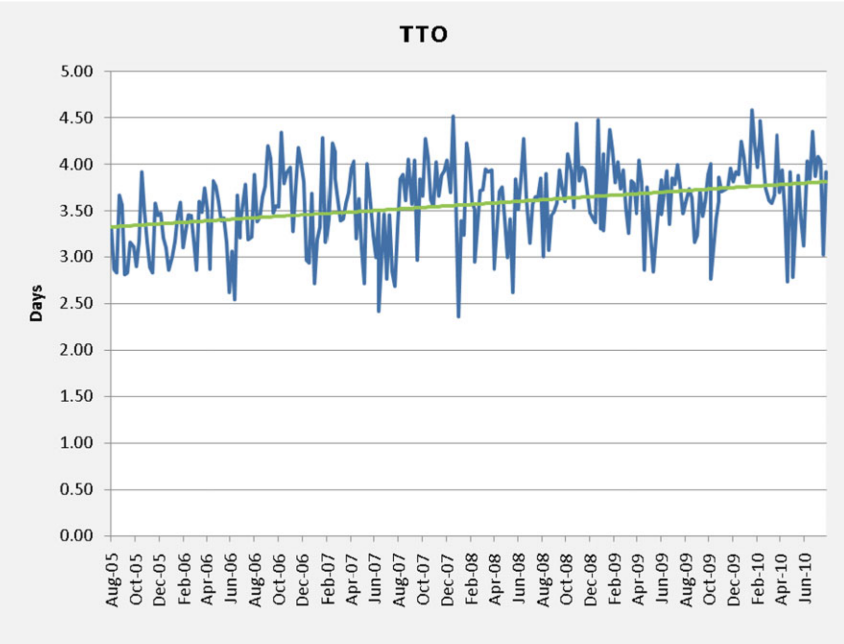

Fig. 3. Actual mean average TTO of PCs per week set against the calendar time as of July 2005. The equation is (standard errors in parentheses): TTO = 3.316 (0.062) days + 0.0019 (0.0004) days × Number of weeks since August 2005.

TABLE 3. Actual outdating percentage and TTO statistics over the 5 consecutive years from August 2005 to July 2010

Factor	Year 1	Year 2	Year 3	Year 4	Year 5
Outdating percentage					
Mean (SD)	5.2 (7.1)	2.8 (3.0)	1.5 (2.1)	1.0 (1.5)	1.3 (1.9)
Median (range)	2.8 (0.0-36.5)	2.2 (0.0-13.2)	0.5 (0.0-10.9)	0.5 (0.0-7.5)	0.5 (0.00-7.4)
$Year_n$-$Year_{n-1}$					
Δ Median		–0.6	–1.7	–0.07	–0.02
Z value/p value (U test)		–2.09/0.073	–2.82/0.005	–1.11/0.265	–0.08/0.939
$Year_n$-$Year_1$					
Δ Median		–0.6	–2.3	–2.3	–2.3
Z value/p value (U test)		–2.09/0.073	–4.91/0.000	–5.98/0.000	–5.56/0.000
TTO (days)					
Mean (SD)	3.26 (0.33)	3.52 (0.47)	3.64 (0.42)	3.67 (0.37)	3.73 (0.41)
Δ Mean (95% CI)					
$Year_n$-$Year_{n-1}$		0.26 (0.11-0.42)	0.12 (–0.05 to 0.29)	0.03 (–0.12 to 0.19)	0.06 (–0.09 to 0.22)
$Year_n$-$Year_1$		0.26 (0.11-0.42)	0.38 (0.24-0.53)	0.41 (0.28-0.55)	0.48 (0.33-0.62)

Third, shortages were quite high due to some "overkill" when PCs are bought from other regions. In five instances as much as 30 PCs were bought—"just to be sure"—instead of just a few as warranted by TIMO.

Fourth, in decision making on the number of PCs to be produced, the production department must also take into account expected losses for other reasons than outdating. Here again, in practice production levels were sometimes exceeded "just to be sure." However, panic purchases or ad hoc changes in order-up-to rules should be avoided. They act like a boomerang and are likely to bring along both increased outdating and increased shortages later on.

To illustrate this effect, consider the following hypothetical case (see Fig. 4). On a Tuesday, in a blood bank a panic-driven purchase and production took place leading to a high initial inventory level that week. If the blood bank produces PCs in compliance again with the order-up-to rule for the rest of the week, no extra PCs will be produced. The next Tuesday a problem arises, because all remaining PCs, produced the preceding Tuesday, become outdated, bringing an inventory level of zero PCs and selling "no" to become reality. That is, if no further actions are taken. An even worse result in this case might be a repetitious course of actions in the week(s) to come. Here, TIMO showed to be a tutor for the blood banking inventory management. The visualized results acted as a reassurance for those being responsible for the inventory level and production levels. TIMO calculates the likelihood of subsequent events. Of course, there is no 100% guarantee that the next demand is not totally different from any prediction. Nevertheless, many emotion-driven decisions could be avoided.

Improvement in outdating rates and shortages can be reached through economy of scale. The coefficient of variation (CV) in demand generally correlates negatively with the absolute level in demand. In other words, when the absolute level in demand is high, for example, more than 10,000 PCs per year, the CV in daily demand is lower due to leveling off effects. Then again, high levels of demand are likely to bring along a large service area with its subsequent logistic problems—including the need for more than one distribution point, or an in-hospital inventory, and increasingly complex transportation systems. We intend to widen our research taking these circumstances into consideration.

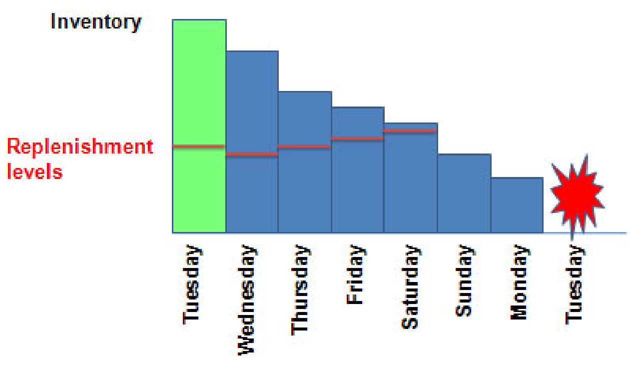

Fig. 4. This exaggerated example illustrates a line of events that might happen if the current order-up-to is violated. The panic-driven production and/or purchase of PCs on some Tuesday leads to an overshoot in the inventory level. Subsequently, again complying with the order-up-to rules—in this blood bank that does not produce PCs on Sundays and Mondays—could result in outdating and a shortage on the next Tuesday.

In the opposite situation, if for example the reference area of the blood bank is small, there will be lower levels of demand and, often, the CV of the demand will be higher. As a consequence, SDP/S results on outdating and/or shortage percentage will be higher but still relatively low as was illustrated in the article by Van Dijk and coworkers.[8] In these situations still the SDP/S approach is expected to yield optimal order-up-to levels.

Some circumstances, not applicable to the situation in the Sanquin Blood Bank Southeast Region, can be of consequence for PC inventory management. Importantly, in many countries a shorter accepted shelf life exists. With the Sanquin Blood Bank Southeast Region production scheme with only 5 production days and an allowed shelf life of 4 days, SDP/S modeling predicts an outdating percentage of somewhat more than 5% with a concurrent shortage percentage of 0.8%. Modeling an expansion of production days to 7—with a production capacity of 40 PCs on Saturday, Sunday, and Monday—showed that this could theoretically be brought down to an outdating percentage of 0.7% and a shortage percentage of less than 0.1%. Theoretical analysis has shown that reduction of outdating is substantial when shelf life is extended to 5 days.[18] Further extension of the shelf life to 6 or 7 days does lead to lower outdating rates progressively, however, with a concurrent (small) increase in the mean PC age at the time of issue.

Another aspect that could influence the inventory management results is increasing the production of PCs through apheresis. Production costs set aside, the improvement would be the earlier availability of PCs, where laboratory results—in particular nuclear amplification testing results—would be the time-limiting factor for this availability. Subsequently, earlier availability would prolong the time for issuing. We have not made any calculations for this situation, but anticipate that SDP/S modeling would, if anything, bring about further improvement.

CONCLUSION

Theory learns that calculated inventory management of PCs could lead to very low numbers of outdating and shortages, but certainly has its limitations. Variance in demand is high and production capacity is not infinite, while logistic constraints do turn up when trying to get economy of scale. Still, applying the theory may help a blood bank to improve its inventory management substantially and may help to identify to what extent practical limits may come close to theoretical limits. More importantly, reassurance of personnel at the blood bank by objective calculations and simulation helps avoiding adhocracy by producing or purchasing costly products without added value or even bringing about product losses. Our results illustrate these possibilities.

REFERENCES

1. Veihola M, Aroviita P, Linna M, Sintonen H, Kekomaki R. Variation of platelet production and discard rates in 17 blood centers representing 10 European countries from 2000 to 2002. Transfusion 2006;46:991-5.
2. Pinson SD, Pierskalla WP, Schaefer B. A computer simulation analysis of blood bank inventory policies. Evanston (IL): Department of Industrial Engineering and Management Sciences, Northwestern University; 1972.
3. McCullough J, Undis J, Allen JW Jr. Platelet production and inventory management. In: Mallory DM, editor. Platelet physiology and transfusion. Washington (DC): American Association of Blood Banks; 1978. p. 17-38.
4. Katz AJ, Carter CW, Saxton P, Blutt J, Kakaiya RM. Simulation analysis of platelet production and inventory management. Vox Sang 1983;44:31-6.
5. Ledman RE, Groh N. Platelet production planning to ensure availability while minimizing outdating. Transfusion 1984;24:532-3.
6. Sirelson V, Brodheim E. A computer planning model for blood platelet production and distribution. Comput Methods Programs Biomed 1991;35:279-91.
7. Hesse SM, Coullard C, Daskin MS, Hurter AP. A case study in platelet inventory management. In: Bidanda B, Jaydale S, editors. Proceedings of the sixth annual industrial engineering research conference. Atlanta: Institute of Industrial Engineers; 1997. p. 801-6.
8. Van Dijk N, Haijema R, van der Wal J, Sibinga CS. Blood platelet production: a novel approach for practical optimization. Transfusion 2009;49:411-20.
9. Pierskalla WP, Roach CD. Optimal issuing policies for perishable inventory. Manag Sci 1972;18:603-14.
10. Nahmias S. Perishable inventory theory: a review. Oper Res 1982;30:680-708.
11. Prastacos GP. Blood inventory management: an overview of theory and practice. Manag Sci 1984;30:777-800.
12. Cohen MA, Pierskalla WP. Management policies for a regional blood bank. Transfusion 1975;15:58-67.
13. Blake JT, Thompson S, Smith S, Anderson D, Arellano R, Bernard D. Using dynamic programming to optimize the platelet supply chain in Nova Scotia. In: Dlouhý M, editor. Proceedings of the 29th meeting of the European Working Group on Operational Research Applied to Health Services. Prague, Czech Republic: ORAHS; 2003. p. 47-65.
14. Curvers J, van Pampus EC, Feijge MA, Rombout-Sestrienkova E, Giesen PL, Heemskerk JW. Decreased responsiveness and development of activation markers of PLTs stored in plasma. Transfusion 2004;44:49-58.
15. Keuren JF, Cauwenberghs S, Heeremans J, de Kort W, Heemskerk JW, Curvers J. Platelet ADP response deteriorates in synthetic storage media. Transfusion 2006;46:204-12.
16. Ross SM. Introduction to stochastic dynamic programming. New York: Academic Press; 1983.
17. Puterman ML. Markov decision processes: discrete stochastic dynamic programming. Wiley Series in Probability and Mathematical Statistics. New York: John Wiley & Sons; 1994.
18. Haijema R, Van der Wal J, Van Dijk NM. Blood platelet production: optimization by dynamic programming and simulation. Comput Oper Res 2007;34:760-79.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1. A brief description of the Thrombocyte Inventory Management Optimizer, TIMO.

Please note: Wiley-Blackwell are not responsible for the content or functionality of any supporting materials supplied by the authors. Any queries (other than missing material) should be directed to the corresponding author for the article.