Impact of implementing pathogen reduction technologies for platelets on reducing outdates

Carlos Gorria,[1] Gorka Labata,[2] Mikel Lezaun,[1] F. Javier López,[3] Ana Isabel Pérez Aliaga,[4] & Miguel Ángel Pérez Vaquero,[5]

[1]*Department of Applied Mathematics, Statistics and Operations Research, University of the Basque Country - UPV/EHU, Bizkaia, Spain*

[2]*Instituto Tecnológico de Aragón, Zaragoza, Spain*

[3]*Department of Statistical Methods and Institute for Biocomputation and Physics of Complex Systems, University of Zaragoza, Zaragoza, Spain*

[4]*Banco de Sangre y Tejidos de Aragón, Zaragoza, Spain*

[5]*Basque Centre for Transfusion and Human Tissues (CVTTH), Galdakao, Bizkaia, Spain*

Background and Objectives Applying pathogen reduction technologies (PRT) to platelets can extend their shelf life from 5 to 7 days, but there have been few systematic studies of the repercussions of such technologies on outdate rates.

Material and Methods The benefits in terms of outdate rates of applying PRT to platelets are studied via a mathematical simulation. Specifically, statistical methods are used to determine the daily production rate needed to meet demand while not exceeding a maximum amount set as a result of limitations on donations and while assuring a minimum daily stock.

Results The results show that a 2-day extension in the shelf life of platelet concentrates (PC) results in reductions in outdates ranging from 88·4% to 100% at the production centres analysed. It may be the case for budgetary reasons that only part of the PCs produced can be treated. This being so, we show that if the proportion treated per annum exceeds 25% the best option is to treat part of the output every day, otherwise, it is preferable to concentrate treatment on the last two production days of the week.

Conclusions Extending the shelf life of PC from five to seven days and setting up suitable production logistics can drastically reduce outdates at production centres. If only a part of all PCs is treated, the best choices are to distribute PRT overall production days or, if the percentage of PCs treated is very low, to apply PRT on the days preceding the weekend break.

Key words: mathematical simulation, optimization, platelet concentrate stocks.

Introduction

Production centres for blood components have the job of supplying hospitals with the products that they need in time and strive to discard as few units as possible during production and due to outdating. In the case of platelet concentrates (PC), it is hard to meet these goals for several reasons. Their short shelf life (a maximum of 5 days, extendable to seven if a bacterial detection method is used or they are treated with a pathogen reduction technology [1]) and growing demand due to an ageing population and increasingly aggressive pharmacological treatments [2].

Pathogen reduction technology (PRT) for PC first emerged at the end of the 20th century to increase pro- tection against infection, since it inactivates viruses, para- sites and bacteria [3–6]. PRT is used in at least 31 countries [7]. This technique allows in some countries, not in all, the shelf life of PC to be extended to seven days and can replace irradiation because it inactivates residual leucocytes [8]. This means lower PC outdate rates [9] and, in turn, provides a major logistical advantage. However, in spite of the studies published on it to date [10–12], its use is not yet widespread due to cost.

Numerous papers have analysed the financial cost of implementing PRT [13–19]. One important aspect of the savings to be made by extending the shelf life of PC to 7 days is the reduction in the number of units discarded due to outdating. Not all papers that examine the issue quantify these reductions [13], and those which do give widely differing figures. For instance, there are references to reductions in outdates of between 30 and 45% based on estimates by staff in charge of production [14]. One study argues that there could be a decrease of 1·6% per additional hour of PC shelf life, which would result in an overall figure of 77% for a 2-day increase [15]. Another recent study [16] mentions a reduction in outdates of 47% with an extension of shelf life from 5 to 7 days, with an outdate rate of 9·5% for 5-day PC and 5% for 7 days. Another paper mentions a 50% reduction in out- dates in the Belgian health system [17]. Girona-Llobera et al. indicate a reduction of 83·9%, based on empirical data from the blood bank in the Balearic Islands (Spain) after 3 years of implementing PRT [18]. The production policy and the source of obtaining the data vary from one region to another and some of the studies using empiric data, comparing results before and after the implementation of PRT, have findings that might be region-specific and therefore not generalizable. The estimates based on expert opinions are subjective, while the reduction in outdates in those based on the actual implementation of the technique could be influenced by factors other than a longer shelf life, given that the implementation process may take

months or years [18]. To the best of our knowledge, the only paper that systematically analyses the reduction in outdate rates when PC shelf life is extended from 5 to 7 days is that of Blake [19]. He examines the transfusion system in Canada, comprising seven production centres and 91 hospitals regularly receiving PCs, and uses Monte Carlo simulation to quantify the reduction in outdating due to extension of shelf life of PCs. He finds that for a 2-day extension in usable shelf life outdating decreases from 8·5% to 7·3% (a 13·5% reduction) at production centres and from 24·2% to 12·9% (46·5% reduction) in the system as a whole. In this article, we use mathematical simulation to present an analysis of outdates at the production centre level. This enables us to assess the results in different settings and with different parametric values for the models. Our paper complements the paper by Blake [19] in several aspects. First, it analyses the reduction in wastage at two production centres where outdates (ranging from 1·4% to 4·5% depending on the scenarios) are much smaller than in Blake [19], thus enabling us to assess the effect of PRT

when the number of outdated units is already very low. We also address several other interesting issues (see points 2 and 3 below) not considered in Blake [19].
Our goal in this paper is to study:
(1) The reduction in outdates when average shelf life is extended from 5 to 7 days.
(2) The increase in the remaining average useful lifetime of PCs when they are dispatched to hospitals.
(3) The effect of distributing treatment across different patterns of production days during the week when only part of the PCs can be treated for budgetary rea- sons.

Materials and methods
The reduction in outdates brought about by extending the shelf life of PC from 5 days to seven is estimated using a mathematical simulation. Two production centres in Spain are considered the CVTTH (Basque Centre for Transfusions and Human Tissue) and the BSTA (Aragon Blood n Tissue Bank). Each is the only production centre in its region. The CVTTH produces 11 500 PCs per annum and the BSTA produces 6200. Both centres produce PCs on only five days each week (Monday to Friday at the CVTTH and Tuesday to Saturday at the BSTA). The main difference between them is in lead time, that is the time between the placing of an order for production and the availability of the product as stock for shipment to hospitals.
In both scenarios, the model parameters are calculated using the data on demand at the BSTA in 2016 (Table 1), taking advantage of the fact that they fit into a normal distribution based on the days of the week. Once the models are defined, they are applied to the real data on demand at BSTA from hospitals in 2017. This results in values for several variables, including the number of out- dates, the minimum daily stock and the average remaining shelf life of PC sent to hospitals. In PC demand and supply data, no distinction is drawn between ABO and Rh groups or between their provenances, apheresis or platelet pools.
As usual in inventory systems which are regularly reviewed, an order-up-to production policy is used. This consists of setting an order-up-to value for each day of the week. Once demand for the day has been met, an order is placed for the production of sufficient PC to reach the order-up-to value for the relevant day of the week. Obviously, if the stock available once demand has been met exceeds the order-up-to value, no further production is ordered.

The order-up-to value is defined as $\mu + k\mathrm{r} + k_i$, where μ and r are the mean and the standard deviation of the demand to be covered by the order, k is un safety factor set to 3 and k_1, k_2 are constants used to increase the safety stock. We use a value of k_1 for the first three production days and k_2 for the last two. These two parameters are included to guard against the possibility that the demand in 2017 may be greater than the estimates calculated using 2016 data. For supplies, a FIFO (first-in, first- out) policy is assumed.

The models are implemented on an easy-to-use Excel spreadsheet. The procedure entails calculating production day by day throughout the year, in line with the demand to be met. Implementation is immediate.

Scenario 1. CVTTH

The CVTTH model shown here can be seen in Pérez- Vaquero et al. [20]. It is a simplification that maintains all the main characteristics of the process currently used at the centre. The PC produced and supplied and the stocks held are accounted for per calendar day. Stocks are updated every morning once outdates have been dis- carded and the latest PC produced are incorporated. There is no production on Saturdays or Sundays.

Orders produced on one day are incorporated into stocks the next day with an age of 1, except in the case of those produced on a Friday, which go into stocks on the following Monday with an age of 3. Thus, for instance,

PCs whose production is ordered on a Monday may be sent to hospitals from Tuesday to Saturday if their shelf life is 5 days, or from Tuesday to the following Monday if it is 7 days. Similarly, PCs whose production is ordered on a Friday can be sent to hospitals from Mon- day to Wednesday if their shelf life is 5 days and from Monday to the following Friday if it is 7 days. Units not dispatched after their last shelf life day are discarded.

The order-up-to value μ + kr + ki for the various pro- duction days in the week is calculated as follows. Given that on Mondays the next production (that of Tuesday) comes into stocks on Wednesday, the order-up-to value for a Monday must cover demand for both Monday and Tuesday. Thus, μ is the mean of the joint demand for Monday and Tuesday, and r is the standard deviation. The same occurs with orders on Tuesdays and Wednesdays. Friday orders are not incorporated into stocks until the following Monday, so the order-up-to value for a Thursday must cover the needs from Thursday to Sunday. Therefore, μ is the mean of the joint demand for those

4 days and r its standard deviation. Similarly, the figure for Fridays is based on the joint demand for Friday to Monday.

Table 2 shows the order-up-to values for each production day of the week, calculated as the relevant mean values plus three times the standard deviation, plus k1 and k2 to assure a safety stock.

In placing the production order for a day, the units in stock at the start of the day are counted and the quantity of PCs required to make up the order-up-to value is requested. However, limitations arising from the number of donations on each day mean that an upper limit of P_{max} is set on production per day. If the quantity needed to reach the upper limit set exceeds the maximum production figure P_{max}, then the latter figure is produced. The figure set in all cases is P_{max} = 30.

Scenario 2. BSTA

The BSTA operates much like the CVTTH. In this case, the production days are Tuesday to Saturday. The main difference with the CVTTH is that no bacterial cultures are carried out, so units whose production is ordered from Tuesday to Friday can be sent to hospitals on the day of their production, with an age of 1. For instance, PCs whose production is ordered on a Tuesday can be sent to hospitals from Tuesday to Saturday if its shelf life is 5 days and from Tuesday to the following Monday if it is 7 days. Units produced on a Saturday become available as stock on Monday, because the laboratory does not run the relevant tests over the weekend. Thus, a unit whose production is ordered on a Saturday can be dispatched from Monday to Wednesday if its shelf life is 5 days and from Monday to Friday if it is 7 days. As in scenario 1, the BSTA also has a limit on the maximum quantity of PCs that can be produced in a day. That limit is denoted by P_{max} and is set at 30.

Except on Saturdays, orders are incorporated into stocks on the day of production, so the order-up-to value for Tuesdays, Wednesdays and Thursdays only needs to meet the needs envisaged for that same day. Those needs are estimated as the mean plus three times the standard deviation of the demand for PC on Tuesdays, Wednesdays and Thursdays, respectively. Given that the next production order (that of Saturday) is incorporated into stocks on Monday, Friday orders must take into consideration the needs from Friday to Sunday. Also, given that the next production order after that of Saturday is that of Tuesday, which comes into stocks on Tuesday, the order- up-to value for Saturday must meet the needs from Saturday to Monday. With these order-up-to values, the quantity to be produced on Saturdays may be very high and may often exceed the maximum production P_{max}, which is set at 30. To correct this shortcoming, production on Fridays is increased beyond the needs for the day to cover part of the needs corresponding to Saturday's production. Thus, Friday's production takes into account the demand for Saturday to Monday, in the knowledge that the maximum quantity of PC set can be produced on Saturday. With this correction, the order-up-to value for Fridays is the mean plus three times the standard deviation for the joint demand for PC from Friday to Monday, minus the maximum production P_{max}. The upper limit for Saturdays continues to be the mean plus three times the standard deviation of the joint demand for Saturday to Monday.

Table 3 shows the values for the mean plus three times the standard deviation which, once k1 and k2 have been added to assure a safety stock, make up the order-up-to value for the production days of the week. As can be seen, the figures are lower than for the CVTTH. This is because here the lead time is 0 for orders on every day except Saturday.

When the production order for a day is placed, the units in stock at the start of the day are counted and the quantity of PC required to make up the order-up-to value is requested, with the maximum production P_{max}.

Results

We now show the results of the simulations carried out in regard to meeting the real demand for PC from BSTA in 2017. The simulation thus replicates the circumstances at the production centre in 2017 if the policy applied were that set for the models obtained with the data for 2016.
With a view to comparing the drop in outdates when PC shelf life is increased from 5 to 7 days in the two scenarios, simulations are conducted in two different set- tings: One with (k1, k2) = (5,0) and the other with (k1, k2) = (15,5). These two pairs of parameters were chosen to show the results of two production policies, one of which is more conservative than the other. The results are shown in Table 4. The 'Min. stock' column shows the minimum daily stock obtained over the whole year. A negative figure means a stock-out. The average remaining lifetime in days' shows the mean remaining lifetime of PCs when they are sent to hospitals. To establish guidelines as to the best days of the week for treating PCs when treatment cannot be conducted every day, three different weekly treatment patterns are compared as follows: distributing PC treatment over all the production days of the week, treating only on the first three production days and treating only on the last two production days. This is done for different percentages of PCs treated as follows: 45%, 25%, 12%, and 6%. Note that a given treatment percentage, for example 25%, means that only that proportion of the PC production per annum is treated. The results are shown in Table 5 for the CVTTH and Table 6 for the BSTA.
In some circumstances there are minimum stocks of a -1, which means that on a particular day there is a short- fall of one PC not delivered to a hospital. Stock-outs in

the distribution of PCs are undesirable, and indeed highly infrequent, but they may occur in specific cases. For example, Blake [21] gives a shortage of 0·49% in the distribution system in Canada. The results are very similar in the two scenarios. The worst option is to concentrate PRT application on the first days of the week. When the proportion of units treated is greater than 25% the best results are obtained when PRT application is distributed across all production days, but if it is less than 25% it is better to concentrate PRT use on the last production days in the week.

DISCUSSION

Since PC treatment techniques were introduced, numerous papers have studied their impact from both clinical and financial (costs and savings) viewpoints. Part of the savings obtained originates from the extension of PC shelf life from five days to seven, which means fewer outdated units. However, there are few systematic studies on the actual reduction in outdates. The figures given in the literature vary from 30% to 86%, and papers have some- times failed to specify whether they refer to production centres, transfusion centres or both. Pérez-Vaquero, et al.
[8] refer to 5·27% differences in outdates at Spanish production centres (3·49% untreated vs. 1·62% treated) while at hospitals the figures range from 0 to 38·7%. Our paper uses mathematical simulation based on actual data to calculate and compare the change in outdate rates when shelf life is extended from 5 to 7 days in a variety of set- tings with different safety stocks and two scenarios associated with two production centres. Our findings indicate that if a reasonable production policy is followed then the shift from 5 to 7 days enables outdates to be almost entirely eliminated (the reductions obtained range from 88% to 100%). This contrasts with the paper by Blake [19], who finds an expected reduction of 13·5% at production centres and 46·5% for the system as a whole in the Canadian transfusion system when usable shelf life is extended by two days. By contrast, McCullogh [14] gives much lower outdate rates, though it must be taken into account that the percentages of reduction in the paper in question are estimates by heads of production centres and are not therefore based on empirical data. The results presented here are consistent with other papers such as that of Girona, et al. [18], who indicate an 86% reduction in outdate rates. As can be seen in Tables 4–6, the outdate rates are lower in scenario 2, where reductions of up to 100% are obtained when treated platelets are used. This is because the production system at this centre is more efficient in terms of logistics than the one in scenario 1, since the lead time is zero for some days of the week.
The second objective of the paper is to analyse how
the increase in the shelf life of PCs at production centres translates into an increase in their remaining lifetime when they are dispatched to hospitals [21,22]. The figures in the last column of Table 4 show that there is an increase of almost two days (ranging from 1,7 days at CVTTH with (k1, k2) = (15,5) to 1·91 days at BSTA with (k1, k2) = (5,0) in the remaining lifetime of PCs shipped

by centres when shelf life is extended from 5 to 7 days. Therefore, the use of PRT will result in PCs arriving at hospitals with almost two more days of remaining life- time. This means that not just reductions in wastage at

production centres but also a subsequent reduction in outdating at hospitals are to be expected.
Another goal of this study is to provide answers for production centres that wish to incorporate PRT but cannot apply it to their entire output for budgetary reasons. This raises doubts as to whether it is better to apply PRT to a set percentage of PC units every day or concentrate treatment on certain days of the week. The comparison of different treatment patterns conducted here reveals that to minimize outdate rates it is better to distribute treatment over all days when more than 25% of PCs are PTR- treated. However, if only 25% of units or less are to be treated, it is better to concentrate treatment on the last few days of the week, just before production stops for the weekend. In any event, the worst option is to concentrate treatment on the early days of the week. There are, of course, many factors which can influence this decision, such as the availability of technical staff and the need to have new treated PC units available every day. We are aware that the availability for transfusion of two types of PCs with different safety levels may raise ethical and legal questions which are difficult to answer. That said, this paper focuses strictly on the logistics of production and distribution.
This study considers only production centres. A more comprehensive study would cover the whole transfusion system, including both production centres and hospitals. This would require a good information system so as to provide a complete database with data on production and transfusions. Outdating at hospitals can also vary widely depending on a number of factors, such as size, uses of PCs, geographical location, logistics, etc. We have focused on production centres because results are easier to extrapolate to other regions or countries. As commented above, the almost two-day increase in the remaining lifetime of PCs on arrival at hospitals means a substantial reduction in wastage there. This is consistent with the results in Pérez-Vaquero, et al. [8], which show that outdate rates at hospitals drop when PCs expire after seven days.
We do not distinguish between ABO and Rh groups; the results in Blake [19] show that the effect of blood type is not significant, that is the reduction in wastage is similar in all blood groups. Another limitation of our study, albeit a minor one, is that the model follows a strict FIFO (first-in, first-out) supply policy. In practice, this is not always how things work: There are situations in which the patient needs irradiated PC and the unit used for the transfusion is not the closest to its expiry date.

Sources of support
Mikel Lezaun and Carlos Gorria have received funding from the European Union's Horizon 2020 research and innovation program under the Marie Sklodowska-Curie grant agreement no. 777778 (MATHROCKS), the Project of the Spanish Ministry of Economy and Competitiveness with

reference MTM2016-76329-R (AEI/FEDER, EU) and the Bas- que Government through the two Elkartek projects ArgIA (KK-2019-00068) and MATHEO (KK-2019-00085), and the
Consolidated Research Group MATHMODE (IT1294-19), given by the Department of Education. The contribution of
F. Javier López has been partially funded by the Ministry of Economy and Competitiveness (MTM2017-83812-P).

References

1 Council of Europe. European Directorate for the Quality of Medicines fl Health Care. Guide to the Preparation, Use and Quality Assurance of Blood Components. 19th edn. Strasbourg, France: Council of Europe, 2017
2 Desborough MJ, Smethurst PA, Est- court LJ, et al.: Alternatives to allogeneic platelet transfusion. Br J Haematol 2016; 175:381–392
3 Lin L, Dikeman R, Molini B, et al.: Photochemical treatment of platelet concentrates with amotosalen and long-wave length ultraviolet light inactivates a broad spectrum of pathogenic bacteria. Transfusion 2004; 44:1496–1504
4 Lin L, Hanson CV, Alter HJ, et al.: Inactivation of viruses in platelet concentrates by photochemical treatment with amotosalen and long wave length ultraviolet light. Transfusion 2005; 45:580–590
5 Ruane PH, Edrich R, Gampp D, et al.: Photochemical inactivation of selected viruses and bacteria in platelet concentrates using riboflavin and light. Transfusion 2004; 44(6):877–885
6 Goodrich RP, Edrich RA, Li J, et al.: The Mirasol PRT system for pathogen reduction of platelets and

plasma: an overview of current status and future trends. Transfus Apher Sci 2006; 35:5–17
7 AABB. Listing of countries in which pathogen reduction technology systems and products are in use. 2015. https://www.aabb.org/tm/eid/Documents/Prt-systems-inuse-country-listing./ pdf
8 Marschner S, Fast LD, Baldwin WM III, et al.: White blood cell inactivation after treatment with riboflavin and ultraviolet light. Transfusion 2010; 50:2489–2498
9 Pérez-Vaquero M, Gorria C, Lezaun M, et al.: Boletín SETS 2012; n° 82:23(1)
10 van der Meer PF, Ypma PF, van Gelo- ven N, et al.: Hemostatic efficacy of pathogen –inactivated vs untreated platelets: a randomized controlled trial. Blood 2018; 132:223–231
11 Estcourt LJ, Chir B, Malouf R, et al.: Pathogen-reduced platelets for preven- tion of bleeding in people of any age. JAMA Oncol 2018; 4:571–572
12 Garban F, Cuyard A, Labussiere H, et al.: Comparison of the hemostatic efficacy of pathogen-reduced platelets vs untreated platelets in patients with thrombocytopenia and malignant hematologic diseases: a randomized clinical trial. JAMA Oncol 2018; 4:468–475
13 Cicchetti A, Coretti S, Sacco F, et al.: Budget impact of implementing plate- let pathogen reduction into the Italian blood transfusion system. Blood Transfus 2018; 16:483–487
14 McCullough J, Goldfinger D, Gorlin J, et al.: Cost implications of implementation of pathogen-inactivated plate- lets. Transfusion 2015; 5:2312–2320
15 Prioli KM, Karp JK, Lyons NM, et al.: Economic implications of pathogen reduced and bacterially tested platelet components: a US Hospital Budget Impact Model. Appl Health Econ Health Policy 2018; 1–11
16 Kacker S, Bloch EM, Ness PM, et al.: Financial impact of alternative approaches to reduce bacterial con- tamination of platelet transfusions. Transfusion 2019; 59: 1291–1299
17 Moeremans K, Warie H, Annemans L: Assessment of the economic value of the INTERCEPT blood system in Belgium. Transfusion Med 2006; 16:17–30
18 Girona-Llobera E, Jimenez-Marco T, Galmes-Trueba A, et al.: Reducing the financial impact of pathogen inactivation technology for platelet components: our experience. Transfusion 2014; 54:158–168
19 Blake JT: Determining the inventory impact of extended-shelf life platelets with a network simulation model. Transfusion 2017; 57:3001–3008
20 Pérez Vaquero MA, Gorria C, Lezaun
M, et al.: Optimization of the management of platelet concentrate stocks in the Basque Country using mathematical simulation. VoxSanguinis 2016; 110:369–375
21 Cardigan R, Williamson LM: The quality of platelet after storage for 7 days. Transfusion Med 2003; 13:173–187
22 Cid J, Escolar G, Lozano M: Therapeutic efficacy of platelet components treated with amotosalen and ultraviolet A pathogen inactivation method: results of a meta-analysis of randomized controlled trials. Vox Sang 2012; 103:322–330

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Mean	21.0	18.8	19.4	22.5	22.0	6.6	7.7
Standard deviation	6.1	5.9	5.3	6.0	6.3	3.4	3.5

Table 1. Mean and standard deviation for daily demand for PC at BSTA (2016)

	Mon +Tue	Tue +Wed	Wed +Thu	Thu + Fri + Sat + Sun	Fri + Sat + Sun + Mon
Mean + 3 × standard deviation	65	61	65	91	90
	Monday	Tuesday	Wednesday	Thursday	Friday
Order-up-to value	65+ k_1	61+ k_1	65+ k_1	91+ k_2	90+ k_2

Table 2. CVTTH modus operandi. Mean values plus three times the standard deviation for the PCs supplied by the BSTA in 2016 in different groupings of days of the week, and order-up-to values for each production day of the week. In the examples $(k_1, k_2) = (5,0)$ *and* $(k_1, k_2) = (15,5)$.

	Tuesday	Wednesday	Thursday	Fri +Sat + Sun + Mon	Sat + Sun + Mon
Mean + 3 × standard deviation	37	37	41	84	76
	Tuesday	Wednesday	Thursday	Friday	Saturday
Order-up-to value	37+ k_1	37+ k_1	41+ k_1	84- P_{max} + k_2	76+ k_2

Table 3. BSTA modus operandi. Mean plus three times the standard deviation for PC supplied by the BSTA in 2016 in different groupings of days of the week, plus the order-up-to values for each production day of the week. In the examples $P_{max} = 30$, $(k_1, k_2) = (5, 0)$ *and* $(k_1, k_2) = (15, 5)$.

Scenario	Parameters	Shelf life	PC Produced	Outdates	Outdate %	Reduction in outdate rate	Min. stock	Average remaining lifetime in days
1. CVTTH	$(k_1, k_2) = (15, 5)$	5 days	6.107	138	2,26%		0	1,89
		7 days	5.990	16	0,27%	88,4%	0	3,73
	$(k_1, k_2) = (15, 5)$	5 days	6.262	284	4.54%		8	1,55
		7 days	5.995	16	0,27%	94,4%	10	3,23
2. BSTA	$(k_1, k_2) = (5, 0)$	5 days	6.096	86	1,41%		0	1,99
		7 days	6.010	0	0,00%	100,0%	0	3,90
	$(k_1, k_2) = (15, 5)$	5 days	6.199	184	2,97%		10	1,56
		7 days	6.016	1	0,02%	99,5%	10	3,39

Table 4. Comparison between five and seven day shelf life in scenarios 1 and 2.

Parameters	Days of treating	% PCs treated	Outdate %	Min. stock	Average remaining lifetime in days
$(k_1, k_2) = (5, 0)$	Mon to Fri	45%	0,27%	0	2,72
	Mon to Wed		2,05%	-1	2,87
	Thu and Fri		0,42%	0	2,71
	Mon to Fri	25%	0,62%	0	2,24
	Mon to Wed		2,05%	-1	2,38
	Thu and Fri		0,42%	0	2,24
	Mon to Fri	12%	1,03%	0	2,05
	Mon to Wed		2,15%	-1	2,13
	Thu and Fri		0,63%	0	2,02
	Mon to Fri	6%	1,52%	0	1,96
	Mon to Wed		2,16%	0	2,01
	Thu and Fri		1,11%	0	1,92
$(k_1, k_2) = (15, 5)$	Mon to Fri	45%	0,48%	10	2,17
	Mon to Wed		3,77%	4	2,46
	Thu and Fri		1,26%	10	2,21
	Mon to Fri	25%	1,29%	10	1,77
	Mon to Wed		3,94%	8	1,99
	Thu and Fri		1,26%	10	1,76
	Mon to Fri	12%	2,40%	10	1,64
	Mon to Wed		4,09%	8	1,78
	Thu and Fri		1,65%	10	1,57
	Mon to Fri	6%	3,55%	10	1,58
	Mon to Wed		4,26%	8	1,66
	Thu and Fri		2,75%	10	1,52

Table 5. Scenario 1 (CVTTH). Comparison of the different weekly treatment patterns with various parameter values and PRT percentages.

Parameters	Days of treating	% units treated	Outdate %	Min. stock	Average remaining lifetime in days
$(k_1, k_2) = (5, 0)$	Tue to Sat	45%	0,00%	0	2,92
	Tue to Thu		1,36%	0	3,01
	Fri and Sat		0,00%	0	2,91
	Tue to Sat	25%	0,15%	0	2,44
	Tue to Thu		1,36%	0	2,51
	Fri and Sat		0,00%	0	2,42
	Tue to Sat	12%	0,55%	0	2,21
	Tue to Thu		1,36%	0	2,26
	Fri and Sat		0,15%	0	2,19
	Tue to Sat	6%	0,87%	0	2,09
	Tue to Thu		1,41%	0	2,12
	Fri and Sat		0,56%	0	2,08
$(k_1, k_2) = (15, 5)$	Tue to Sat	45%	0,02%	10	2,35
	Tue to Thu		2,89%	10	2,55
	Fri and Sat		0,20%	10	2,37
	Tue to Sat	25%	0,56%	10	1,91
	Tue to Thu		2,96%	10	2,06
	Fri and Sat		0,20%	10	1,90
	Tue to Sat	12%	1,33%	10	1,72
	Tue to Thu		2,97%	10	1,81
	Fri and Sat		0,59%	10	1,69
	Tue to Sat	6%	2,00%	10	1,64
	Tue to Thu		2,97%	10	1,68
	Fri and Sat		1,44%	10	1,60

Table 6. Scenario 2 (BSTA). Comparison of the different weekly treatment patterns with various parameter values and PRT percentages.