Preparation of chemotherapy drugs: planning policy for reduced waiting times

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Abstract

This study investigates the impact of pharmacy policies on patient waiting time in the Chemotherapy Day Unit of the Netherlands Cancer Institute- Antoni van Leeuwenhoek hospital (NKI-AVL). The project evaluated whether a reduction in waiting time resulting from medication orders being prepared in advance of patient appointments was justified, given that medications prepared in advance risked being wasted if patients arrived too sick for treatment. Within this context, we derive explicit expressions to approximate patient waiting times and wastage costs allowing management to see the tradeoff between these two metrics for different policies. Using a case study and a simulation model, the approximations are evaluated. The explicit expressions allow the analysis to be easily repeated when medication costs change or when new medications/protocols are introduced. In the same vein, other hospitals with different patient case mixes can easily complete the analysis in their setting. Finally, the outcome from this study resulted in a new policy at the cancer centre which is expected to decrease the waiting time by half while only increasing pharmacy’s costs by 1-2%.

Keywords: Stochastic Modelling, Queueing Systems, Pharmacy, Chemotherapy

1 Introduction

Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL) is a comprehensive cancer center, which provides hospital care and research and is located in Amsterdam, The Netherlands. The hospital has 150 inpatient beds and sees about 24,000 new patients every year, making it approximately the size of a mid-sized general hospital. As with many Dutch hospitals, in order to improve quality of care and to increase their capacity, there is a trend toward providing more care in ambulatory (or outpatient) settings. To accommodate the increasing volumes, outpatient departments are being asked to examine their current operations to find ways to improve their department’s efficiency.

To this end, NKI-AVL has completed a number of studies of their chemotherapy day unit (CDU). The CDU is a 30 bed outpatient department where patients receive...
chemotherapy treatment. A course of treatment typically requires weekly or bi-weekly recurring appointments over a number of months. Improvements at this CDU have been reported on before. In work by [6], process improvements allowed more patients to be treated using the same number of beds without increasing the workload. Another study [11] investigated how pooling resources would impact access times. The CDU is also concerned over long waiting time for patients after their arrival at the hospital. Initial analysis indicated that a large percentage of this wait was due to patients waiting for their chemotherapy medication order to be completed by the pharmacy. We describe this process by which medication orders are placed and completed and use operational research models to evaluate how changes affect the cost for the pharmacy and the waiting time for the patients. The relationship between the pharmacy and the CDU is described below.

Patients receiving chemotherapy do so over a number of months with weekly or bi-weekly appointments. Each appointment is scheduled at least one week in advance. On the day of their appointment a patient either reports directly to the CDU or to the laboratory. Patients reporting to the laboratory require a blood test, which is used to assess if they are healthy enough (i.e. fit) to receive their scheduled course of chemotherapy. Patients that are fit receive the chemotherapy, those that are not, are rescheduled for a later time. In this case study we found that approximately 80% of the patients require a blood test and approximately 10% of them are found to be unfit to receive chemotherapy. Patients reporting directly to the CDU will receive a quick health check before receiving the chemotherapy. Approximately 5% of these patients are found to be unfit.

With a few exceptions, current practice states that chemotherapy medications are not to be prepared until after the patient is deemed ‘fit’ to receive treatment and, is present in the CDU. This practice of preparing the medication ‘on demand’ is motivated by the high cost of many of the medications. The pharmacy does not wish to prepare a medicine before they are sure the patient can receive it, as this ensures no medicines are wasted. They argue that since chemotherapy medications can cost up to 1800 euros per treatment, it is prudent to be sure they will be used before preparing them. Indeed, unused medicine may contribute considerably into the operational waste of a hospital [1].

Management of the CDU on the other hand, is concerned that to prepare the medicines ‘on-demand’ adds an extra process step that leads to unnecessary waiting for the patients. For example, CDU management would prefer if the medications were prepared ‘in advance’ of the appointment so that patients could receive their chemotherapy immediately after they have been found fit to receive it. They argue that the percentage of patients found to be unfit is sufficiently low to justify making medications in advance.

To determine which (if any) medication should be made in advance a number of additional factors should be considered. Different medications have different shelf lives which can dictate how soon in advance of an appointment a medicine can be prepared. Different medications have different costs; generic drugs are significantly cheaper than brand name drugs and those which are new. Some medications are more ‘toxic’ which results in a higher percentage of unfit patients. Finally some medications are used more frequently than others which allows them to be given to a different patient, should the original patient be found to be unfit. Because of these many factors and the uncertainty involved in this process, it is unclear to management which medicines should be made ‘in advance’ and which medicines should be made ‘on demand.’

The purpose of this paper is two fold. First as a case study at NKI-AVL, we wish to define a policy stating which medicine should be made in advance. This policy should strike a balance between the cost of wasted medicines and the ‘cost’ of waiting patients. The
second purpose is to describe and evaluate an analytical model with explicit expressions that allows this analysis to be easily repeated at other hospitals.

Using operational research models to improve outpatient clinics is not new; however the majority of studies focus on patient scheduling [2]. Improvements related to operational processes have seen less attention, and in particular, models considering process of two interacting departments are uncommon [5, 12]. Most closely related to the work presented in this paper is by [8] where the authors use a system dynamics simulation to study cost and waiting times for a wide range of chemotherapy patient and drug types. Whereas our model is used to define a policy to guide daily decision making by pharmacists, their model considers how different chemotherapy delivery protocols affect patient satisfaction and costs.

This paper contributes to the growing literature of health care management science through the derivation of explicit expressions for patient waiting times and medication costs, within the described context. Although this context is a specific operational area, the problem is solved conclusively. The explicit expressions have the distinct advantage over simulation techniques in that changes in model parameters can easily be accounted for without needing to repeat model “runs”. Furthermore specific software and trained modellers are not needed to repeat the analysis when medication costs change or when new medications/protocols are introduced. In the same vein, other hospitals with a different patient case mix can easily complete the analysis in their setting without specific software or simulation knowhow.

The paper is organized as follows: the queueing system and model are introduced in Section 2, the waiting time analysis in Section 3, and the analysis of the cost of wasted medication orders in Section 4. The use of the model for policy decisions at NKI-AVL is discussed in Section 5 and a general discussion on the model’s applicability to other other hospitals is discussed in Section 6.

2 Model

The process introduced in the previous section is analyzed by both simulation and analytics. In this paper we describe the analytical model (which is an approximation) in detail, and use a discrete event simulation of the same system to compare numeric results.

2.1 Model Flow

*The queueing system for medication orders in the pharmacy is described as follows:* The system consists of two queues leading to a server with \( c \) pharmacists. Orders \( O_1 \) go to the first queue and wait there until being prepared. These orders are started only after their corresponding patient is deemed fit and must be finished by the end of the day. Orders \( O_2 \) go to the second queue and are not required to be completed this day. These are the orders for patients that will arrive to the hospital on the next day. At the end of each day orders that are still present in the second queue, join the first queue the next day. These orders are called the ‘backlog’ and are denoted by \( L_t \). Orders in the first queue have (non-preemptive) priority over orders in the second queue, since their corresponding patients are waiting. Simply put, \( O_1 \) orders are those that are completed when the patient arrives to the hospital (and is deemed fit for treatment) and \( O_2 \) orders are made in advance of the patient’s arrival.
The queueing system for patients in the CDU is described as follows: Upon arrival it is determined if patients are fit to receive their scheduled treatment of chemotherapy. Unfit patients are sent home without receiving treatment. Fit patients whose medicine orders are part of the ‘completed orders’ immediately receive the treatment. Fit patients whose medicine orders are not part of the ‘completed orders’ must wait until their medication order is complete before receiving treatment. Figure 1 depicts the flows of orders and patients.

![Figure 1: The process model](image)

The decision required in this problem is to determine which medicines should be denoted as $O_1$ orders and conversely, which should be denoted as $O_2$ orders. This decision is evaluated based on the resulting waiting time for patients (Queue 3 from Figure 1) and the expected cost of wasted medicines (medicines prepared in advance for patients who are later found to be unfit to receive their treatment).

In our discrete event simulation we model the system exactly as described above and evaluate each decision as a “what if” scenario. Analytically the system cannot be described straightforwardly as it contains two time scales. Orders arrive during the whole day and their waiting times are measured in minutes. The backlog on the other hand, occurs only at the end of the day creating arrivals to Queue 1 on the next day.

In order to analyze the waiting time in this model analytically we split it into two submodels. The first submodel observes the process on a day-to-day level and allows us to determine the expected amount of backlog on a day. This submodel is described in Subsection 3.1. Using the expected amount of backlog, and given that the arrival rate at the first queue is known, the waiting times of the patients can be determined, as described in Subsection 3.2. An analytic expression to compute the expected cost of wasted medicines is described in Section 4. Both Sections 3 and 4 conclude with numerical results related to the NKI-AVL case study. The data for this case study is introduced in the following subsection.

### 2.2 Model Data

The total number of patients that arrive on a day $t$ is denoted by $N_t$, $N_t \sim \text{Poisson}(\lambda)$ following from the data. In this case study $\lambda = 69.9$. A workday of the pharmacy consists of 555 minutes, starting at 08:15h and ending at 17:30h. The chemotherapy appointments start in batches every fifteen minutes from 08:15h until 15:30h. Thus, the arrival of chemotherapy drug orders are spread over the period $T = 450$ minutes.
the data we derived that the number of arrivals at a fifteen minute time slot $\tau$ has a Poisson($q_{\tau} \cdot \lambda$) distribution, where $q_{\tau}$ is an estimated fraction of patients that arrive at this time slot. Patients require a blood test with probability 0.8. Patients are found to be unfit for treatment with probability 0.1, in the case they had a blood test, and with probability 0.05, otherwise. This results in the fraction $r = 0.8 \times 0.1 + 0.2 \times 0.05 = 0.09$ of unfit patients. In our case study we found this fraction to be the same for each type of medicine, although in general it does not need to be.

Let the set of all 52 medicines be denoted by $S$. The set of medicines that are not allowed to be made in advance (i.e. are $O_1$ orders) is denoted by $S_1$. The set of medicines that are allowed to be made in advance (i.e. are $O_2$ orders) is denoted by $S_2$. We assume that each patient requires medicine $i \in S$ with probability $p_i$ independently of other patients. It follows that the number of patients that need medicine $i$ is Poisson($\lambda \cdot p_i$) distributed. The probability $p_i$ is determined as follows

$$p_i = \frac{f_i}{\sum_{j \in S} f_j},$$

where $f_i$ is the number of times medicine $i$ was used in a year and varies between 1 and 2941. These numbers follow from the data of the hospital. The price of a medicine $i$ is denoted by $c_i$ and is ranging from 1.00 to 1756.99 euros per order.

The preparation times of the medicines are independent and identically distributed and are denoted by $B$, which is uniformly distributed between 5 and 20 minutes, as per the prediction of the pharmacists. The pharmacy is staffed by $c = 2$ pharmacists.

Medicine orders arrive at the pharmacy 24 hours before the appointment time of that patient. The total number of orders that arrive on day $t$ at the pharmacy is denoted by $O_t$. The arriving orders are divided according to a given policy in $O_1^t$ and $O_2^t$. Where $O_1^t$ corresponds to medicines in set $S_1$ and $O_2^t$ corresponds to medicines in $S_2$.

### 3 Patient Waiting Times

#### 3.1 Backlog

In this subsection we describe a slotted queueing model to calculate the expected amount of backlog. Let $L_t$ be the amount of backlog on day $t$, this $L_t$ depends on the number of orders $O_1^t$ and $O_2^t$, the amount of backlog on the previous day $L_{t-1}$ and the capacity of the pharmacy $K_t$. The capacity of the pharmacy is the maximum number of orders that can be made on a day. This slotted model does not take the arrival time of the patients into account, only the orders, which arrive in a batch the day before the patient arrives. It is clear that the sum of $L_{t-1}$, $O_1^t$ and $O_2^t$ equals the total number of orders that need to be handled on day $t$, so the following equation arises

$$L_t = (L_{t-1} + O_1^t + O_2^t - K_t)^+, \tag{1}$$

where $x^+ = \max\{x, 0\}$. Note that since each order has one corresponding patient then

$$O_1^t + O_2^{t-1} = N_t. \tag{2}$$

Assume that on each day the fraction $\sum_{i \in S_2} p_i$ of orders is allowed to be made in advance. Then $O_2^{t-1}$ and $O_2^t$ are identically Poisson distributed with parameter $\lambda \cdot \sum_{i \in S_2} p_i$. Following the model assumptions $O_2^t$ is independent of $O_1^t$. Since the expected number of
patients is the same each day, also the following holds

\[ O_t^1 + O_t^2 = O_t^d = N_t, \]

Furthermore we make the natural assumption that the \( O_t \) is independent of \( K_t \), then equation (1) can be written as

\[ L_t = (L_{t-1} + O_t - K_t)^+. \] (3)

Equation (3) is known as Lindley’s equation (see e.g. [3]). A way to approach a solution of the Lindley equation is by directly solving the corresponding Markov chain. The states of this Markov chain are defined by the number of backlog orders. The transition probabilities of this Markov chain are given by

\[
\begin{align*}
P_{ij} &= \begin{cases} 
\sum_{k=i}^{\infty} P(O_t \leq k - i)P(K_t = k) & \text{if } j = 0, \\
\sum_{k=i-j}^{\infty} P(O_t = j - i + k)P(K_t = k) & \text{if } 0 < j \leq i, \\
\sum_{k=0}^{\infty} P(O_t = j - i + k)P(K_t = k) & \text{if } j > i.
\end{cases}
\end{align*}
\]

Since \( O_t \) is Poisson distributed, we have

\[
\begin{align*}
P_{ij} &= \begin{cases} 
\sum_{k=i}^{\infty} \sum_{j=0}^{\infty} \frac{e^{-\lambda} \lambda^{j-i+k}}{(j-i+k)!} P(K_t = k) & \text{if } j = 0, \\
\sum_{k=i-j}^{\infty} \frac{e^{-\lambda} \lambda^{j-i+k}}{(j-i+k)!} P(K_t = k) & \text{if } 0 < j \leq i, \\
\sum_{k=0}^{\infty} \frac{e^{-\lambda} \lambda^{j-i+k}}{(j-i+k)!} P(K_t = k) & \text{if } j > i.
\end{cases}
\end{align*}
\]

We model \( K_t \) as a normally distributed random variable with mean \( \mu = 87.92 \) and variance \( \sigma^2 = 10.66 \). This follows from the renewal theory result, which implies that the number of independent identically distributed random variables (preparation times) that can be fitted in a large time interval (working day of the pharmacy) is approximately normally distributed with mean and variance defined by the first three moments of the preparation times, see e.g. Ross [9, Chapter 3]. In this case \( P(K_t = k) \) is approximated by \( P(k - 0.5 < K_t < k + 0.5) \). Now to solve the Markov chain, the chain is considered to be finite with \( N \) states, where \( N \) is sufficiently large such that the probability to transit to states larger than \( N \) is negligible. The expected number of backlog orders (\( E[L] \)) follows from the steady state distributions.

### 3.2 Waiting times

Knowing the amount of backlog, the total number of orders in the priority queue (queue 1) can be determined and the waiting times can then be approximated. We explain the approximation in the following three subsections. In the first subsection, the load on the system resulting from the different order types is determined. In the second subsection, we explain how the batch arrival process can be approximately modelled by independent and identically distributed random variables. This adaptation of the arrival process makes it possible to use existing waiting time approximations to solve our problem. The approximation chosen for our purpose is explained and formulated in the third subsection.
Let the expected waiting time of patients that receive a medicine from set $S_1$ be denoted by $E[W_{S_1}]$. This includes the waiting time until a pharmacist starts working on the order and the preparation time of the medicine. This is the only waiting time of concern in our problem as the patients corresponding to these medicine orders are present and waiting in the hospital.

### 3.2.1 System Load

The pharmacy workload results from the two order types, $O_i^t$, $i = 1, 2$ (see Figure 1). Let $\lambda_i$ be the average number of new orders for each arriving in one day (this excludes possible backlog from the day before). The orders of type $O_1^t$ are made by the pharmacy on day $t$, only if the patient is found fit for treatment which happens with probability $1 - r$. As many $O_2^t$ orders as possible, within the opening hours of pharmacy, are completed on day $t$. Those orders which are not completed due to a shortage of time form the backlog $L$ and are added to $\lambda_1$ on day $t + 1$. Furthermore, all orders arrive during the time period when appointments take place, i.e. time period $T$. Thus, let $\rho$ denote the amount of work offered to the system per minute, then we can write

$$\rho = \rho_1 + \rho_2,$$

where

$$\rho_1 = E[B](\lambda_1 + E[L])(1 - r)/T, \quad \rho_2 = E[B]\lambda_2/T$$

and $B$ is the preparation times of the medicines as introduced in Subsection 2.2.

### 3.2.2 Arrival Process

We suggest to evaluate $E[W_{S_1}]$ using the approximating formulas for the $GI/G/c$ priority queue. Note however that the inter-arrival times in our model are not independent and identically distributed (i.i.d.) because patients arrive in batches, and the size of a batch depends on the corresponding appointment slot. To remedy this, we make two approximation steps. First, we assume that the fraction $q_\tau$ of patients arriving at slot $\tau$ is the same for each $\tau = 1, \ldots, T/d$, where $d$ is the time interval between two appointment slots. Then the number of orders arriving at each slot becomes Poisson($\lambda_{\text{slot}}$), with

$$\lambda_{\text{slot}} = (\lambda_1 + E[L])(1 - r)d/T.$$

Next, we apply a so-called Equivalent Random Method. The idea of this method is in replacing a non-i.i.d. sequence of random variables by i.i.d. random variables with the same mean and variance, see [13] for classical references and [7] for recent applications in health care. Thus, we need to compute the mean and variance of inter-arrival times in our system and substitute these numbers into the approximation for the $GI/G/c$ queue.

Let $A_1, A_2, \ldots$ be inter-arrival times between two subsequent patients. Obviously, $E[A] = d/\lambda_{\text{slot}}$. Next, observe that the inter-arrival time between two patients arriving at the same slot is zero. Hence, the renewal theory argument gives that

$$P(A > 0) = \frac{E[\# \text{non-empty batches in one slot}]}{E[\# \text{patients in one slot}]} = \frac{1 - e^{-\lambda_{\text{slot}}}}{\lambda_{\text{slot}}}. $$

Further, note that if $k - 1$ one slots are empty then the inter-arrival time between two non-empty slots becomes $kd$. Thus, we derive

$$E[A^2] = \frac{1 - e^{-\lambda_{\text{slot}}}}{\lambda_{\text{slot}}^2} \sum_{k=1}^{\infty} (kd)^2 e^{-(k-1)\lambda_{\text{slot}}}(1 - e^{-\lambda_{\text{slot}}}) = \frac{d^2}{\lambda_{\text{slot}}^2} \frac{1 + e^{-\lambda_{\text{slot}}}}{1 - e^{-\lambda_{\text{slot}}}}.$$
Define \( c_X^2 = \text{Var}(X)/(E[X])^2 \). Then the calculations above give

\[
c_A^2 = \frac{E[A^2]}{(E[A])^2} - 1 = \frac{\lambda_{\text{slot}}(1 + e^{-\lambda_{\text{slot}}})}{1 - e^{-\lambda_{\text{slot}}}} - 1.
\]

### 3.2.3 Waiting Time

Now we are ready to provide the approximation for the waiting time in different scenarios. First we consider \( S_1 = S \), this means no medicines are made in advance. Thereafter \( S_1 \) is considered to be a subset of \( S \) such that \( S_2 = S \setminus S_1 \) is non-empty, i.e. some medicines are made in advance.

In case \( S_1 = S \) we have a queueing system with \( c \) servers (pharmacists) and independent identically distributed service times. The number of arrivals per day is \( \lambda = \lambda_1 \), and by definition in this case \( E[L] = 0 \). We evaluate the waiting time of the patients in this queueing system using the approximation from [14] for the average waiting time \( W(GI/G/c) \) in the \( GI/G/c \) queue:

\[
E[W_{S_1}] \approx E[W(GI/G/c)] + E[B]
\]

\[
= E[B]c^{-1} \cdot D/[1 - c^{-1} \cdot \rho] + E[B], \quad \text{if } S_1 = S,
\]

where \( D \) denotes the probability of delay in a \( M/M/c \) queue. The expressions for \( E[W(M/M/c)] \) and \( D \) can be found e.g. in Tijms [10], the latter formula being given by

\[
D = \frac{\rho^c}{c!} \left( 1 - \frac{\rho}{c} \sum_{n=0}^{c-1} \frac{\rho^n}{n!} + \frac{\rho^c}{c!} \right)^{-1}.
\]

In the case where \( S_1 \subset S \) such that \( S_2 = S \setminus S_1 \neq \emptyset \), a priority rule is used. The medicines that are prepared for patients on that same day have priority over the medicines that are prepared for the next day. The non-preemptive priority system is used, because the pharmacists cannot shelve the unfinished medicine and resume preparation later. For this priority system we use the approach of Federgruen and Groenevelt [4], which gives the next approximation formula for the waiting time in the priority queue:

\[
E[W_{S_1}] \approx \frac{c_A^2 + c_B^2}{2} D \cdot c^{-1}/[1 - c^{-1} \cdot \rho_1] + E[B], \quad \text{if } S \setminus S_1 \neq \emptyset.
\]

The numerical results in the next section prove that our analytical approximations give a correct picture concerning the expected waiting times.

### 3.3 Numeric Results

Given that there are \( S \) medications, and that each could be made in advance, then there are \( S! \) different policies to evaluate. However in the interest of having an easily implementable policy, NKI-AVL decided that a simple criteria to identify “make in advance” medicines (i.e. \( O^2_t \) orders) should be used. To this end, the price of the medicine is used as the criteria to indicate which medicines should be made in advance. Specifically, if the price of a medicine is less than \( M \) euros, then the medicine is to be made in advance. This limits
the number of policies to evaluate to at most $S$. When $M = 0$ no medicine orders are made in advance, and when $M = 1000$ all medicine orders (which have shelf life greater than 24 hours and are not extremely expensive) are made in advance. Should a hospital chose a different criteria for defining their policy, the analysis of Subsection 3.2, of course remains valid. In the interest of brevity, the numeric results in this paper are limited to only 9 policies, but include both border policies.

Table 1 shows for a chosen $M$ the resulting $\lambda_1$, the amount of backlog and the expected waiting times of patients. The waiting times computed analytically and with simulation are displayed.

<table>
<thead>
<tr>
<th>Amount made in advance:</th>
<th>$M$</th>
<th>$\lambda_1$</th>
<th>$E[L]$ (simulation)</th>
<th>$E[W_{S_1}]$ (simulation)</th>
<th>$E[W_{S_1}]$ (analytical)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>0</td>
<td>69.9</td>
<td>0.00</td>
<td>46.1</td>
<td>55.89</td>
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<td></td>
<td>10</td>
<td>66.1</td>
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<tr>
<td></td>
<td>20</td>
<td>57.0</td>
<td>0.03</td>
<td>33.7</td>
<td>28.62</td>
</tr>
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<td></td>
<td>30</td>
<td>46.4</td>
<td>0.05</td>
<td>26.3</td>
<td>22.43</td>
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<td></td>
<td>40</td>
<td>34.7</td>
<td>0.07</td>
<td>21.1</td>
<td>19.17</td>
</tr>
<tr>
<td></td>
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<td>22.2</td>
<td>0.08</td>
<td>18.0</td>
<td>17.33</td>
</tr>
<tr>
<td></td>
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<td>0.09</td>
<td>17.3</td>
<td>16.99</td>
</tr>
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<td>500</td>
<td>18.2</td>
<td>0.09</td>
<td>17.2</td>
<td>16.94</td>
</tr>
<tr>
<td>All*</td>
<td>1000</td>
<td>6.3</td>
<td>0.09</td>
<td>15.6</td>
<td>16.13</td>
</tr>
</tbody>
</table>

*All medicines which have shelf life greater than 24 hours and not extremely expensive

The expected volume of backlog increases as more medicines are made in advance. This is in line with the observation that if none of the medicines are made in advance then there are no medicines in the second queue and there will be no backlog. In all cases, patients only have to wait if their medicine was not allowed to be made in advance or if their order was backlogged at the end of the previous day.

It is also not surprising that the waiting times are smallest in the case when most medicines are made in advance. In this case only those people requiring a drug with a shelf life of less than 24 hours wait for their medicine to be prepared. The results show clearly that making more medicines in advance results in lower waiting times. The difference between the numerical and analytical results is due to the two approximations in (4). The first approximation replaces the original batch arrival process with i.i.d. arrivals, which may result in an error of a couple of minutes. Next, we refer to the comments on formula (70) in [14] for the conditions, under which the approximation for $E[W(GI/G/c)]$ is sufficiently precise.

4 Cost of the wasted medicine

The downside of making medicines in advance is that every order that is made in advance has a probability to be wasted, resulting in additional costs for the pharmacy. In this section we formulate an expression to compute the expected cost per day $E[C]$ of wasted medicines for a given Policy $M$. First, we assume that all premade orders are wasted when the corresponding patient is found to be unfit for treatment. In Subsection 4.2 we assume
that these orders can be stored and later given to a different patient.

The expected cost per day \( E[C] \) can be calculated in straightforward manner. Recall that \( S_2 \) denotes the set of medicines that are allowed to be made in advance and let \( c_i \) be the price of medicine \( i \) and \( r_i \) the probability that a treatment with medicine \( i \) is wasted due to a patient being found unfit for treatment. Then the following holds

\[
E[C_{\text{order}}] = \sum_{i \in S_2} (c_i \cdot r_i \cdot p_i) + g \cdot r_i
\]  

(6)

where \( g \) is the non material cost to pharmacy to prepare an order (i.e. overhead costs and staff wages). In the NKI case study \( g = 0 \) (without loss of generality) since there was no intention to reduce the number of pharmacy staff and therefore \( g \) was considered an irrelevant sunk cost.

Knowing the cost per order and the frequency of orders, the expected daily cost can be computed as follows,

\[
E[C] = E[C_{\text{order}}] \cdot E[N_t] = \sum_{i \in S_2} c_i \cdot r_i \cdot p_i \cdot \lambda.
\]  

(7)

4.1 Numeric Results

In Table 2 the expected costs compute by (7) and by simulation are shown for various policies \( M \).

<table>
<thead>
<tr>
<th>Amount made in advance: M</th>
<th>( E[C] ) (simulation)</th>
<th>( E[C] ) (analytical)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>10</td>
<td>1.9</td>
<td>1.9</td>
</tr>
<tr>
<td>20</td>
<td>11.3</td>
<td>11.3</td>
</tr>
<tr>
<td>30</td>
<td>35.4</td>
<td>35.4</td>
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<tr>
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<td>71.2</td>
<td>71.1</td>
</tr>
<tr>
<td>100</td>
<td>124.9</td>
<td>124.9</td>
</tr>
<tr>
<td>200</td>
<td>167.6</td>
<td>167.5</td>
</tr>
<tr>
<td>500</td>
<td>185.4</td>
<td>185.7</td>
</tr>
<tr>
<td>All*</td>
<td>1000</td>
<td>897.1</td>
</tr>
</tbody>
</table>

*All medicines which have shelf life greater than 24 hours and not extremely expensive

It is clear that if everything is made in advance the costs are very high. These high costs motivate the analysis of possible storage of medicines after a cancelled treatment for “reuse” by another patient.

4.2 Reuse of medicines

Reuse of the medicines reduces the cost for pharmacy, since fewer medicines will be wasted. However, given the complications (and possible risks) associated with managing an inventory of “to-be-reused” medicines, it is likely that only expensive and frequently used medicines will be stored for later use; others will be discarded. To investigate the impact
of reusing medicines we use a policy $F$ to indicate which medicines can be stored for later use and which will be discarded. The policy is such that if the expected wasted cost of the medicine is higher than $F$, then it can be reused. Let $E[C_i]$ be the expected wasted cost of medicine $i$ defined as,

$$E[C_i] = c_i \cdot r_i \cdot p_i \cdot \lambda$$

(8)

For a given $M$ and $F$, Table 3 shows the expected cost for the pharmacy computed by (7) under the assumption that all medicines $i$, where $E[C_i] > F$, get reused and thus do not contribute into the waste. This assumption is reasonable since the “reuse” medicines are only wasted if they expire before a subsequent order for that medicine is made. This occurs more often when the probability of a patient requiring medicine $i$ ($p_i$) is low. According to (8), such medicine are not selected for “reuse.” Furthermore, simulated results found this assumption reasonable but have been omitted from the text for brevity. Note that “reused” medicines require approximately the same amount of preparation time by the pharmacists (e.g. to check or adjust the dosage) and therefore the waiting time for patients is independent of $F$.

Table 3: Expected daily cost of wasted medicines for different policies $M$ and $F$

<table>
<thead>
<tr>
<th>Amount made in advance:</th>
<th>$M$</th>
<th>300</th>
<th>100</th>
<th>50</th>
<th>20</th>
<th>10</th>
<th>5</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>10</td>
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<td>1.9</td>
<td>1.9</td>
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<td>1.9</td>
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</tr>
<tr>
<td>20</td>
<td>11.3</td>
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<td>11.2</td>
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<td>1.5</td>
<td></td>
</tr>
<tr>
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<td>35.4</td>
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<td>124.9</td>
<td>124.9</td>
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<td>167.5</td>
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<td>185.7</td>
<td>185.7</td>
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<td>42.3</td>
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<td>252.4</td>
<td>188.0</td>
<td>114.9</td>
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<td>44.6</td>
<td>4.2</td>
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<tr>
<td>All*</td>
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<td>705.2</td>
<td>290.2</td>
<td>225.9</td>
<td>127.8</td>
<td>76.1</td>
<td>44.6</td>
<td>4.2</td>
</tr>
</tbody>
</table>

*All medicines which have shelf life greater than 24 hours

The results in Table 3 confirm the statement that the reuse of medicine reduces the costs of the pharmacy. The more medicines that are stored for reuse the lower the costs are. Based on these results it would be convenient to chose to store every medicine for reuse. The hospital however also needs to take other criteria into account, particularly related to safety requirements and inventory space.

5 Policy Decisions

The numeric results in Tables 1 and 2 show how the decision to make medicines in advance influences both the waiting time for patients and the costs for pharmacy. By showing this tradeoff for different values of $M$ we have allowed the hospital to make an informed decision. In September of 2009, after considering the results presented in this paper, management from the pharmacy and the CDU agreed that the shorter waiting times justified making some medicines in advance. Furthermore they chose to reuse their most expensive medicines. Based on this research the hospital is currently making approximately 80% of
all medicines in advance. In this section we discuss and highlight the improvements from this policy change.

To compare different values of $M$ independent of $F$, Figure 2 plots $M$ as a function of both waiting times and costs. The results from both the simulation and analytic approach are shown. The policies of the hospital in 2008 and 2010 are also shown.

![Figure 2: Costs and waiting times for different policies $M$](image)

Each point on Figure 2 represents a different policy $M$. In general, results from the analytical model give a lower estimate of the waiting times. However the analytical results are close to those obtained by simulation when making multiple medicines in advance. The figure shows clearly that the new policy (Policy 2010) decreases the expected waiting time from 45 minutes to 23 minutes at a cost of €105 per day. It is important to realise that waiting patients occupy a place in the chemotherapy unit, which is an indirect capacity loss. In our case study, a gain of 20 minutes per patient spares about 23 person-hours of waiting at the CDU per day! This capacity can be used for handling more patients, thus yielding obvious benefits for the hospital and/or ensuring a high service level such that the patients receive their appointments without delay [11]. On the other hand, the cost bared by the pharmacy is reasonable considering that the pharmacy prepares almost €8,000 worth of medicines per day, meaning the new policy accounts for only a 1-2% percent increase in its costs.

Figure 3 also plots $M$ as a function of both waiting times and costs. The difference however is that in Figure 3, we consider a policy $F \approx 20$ such that the most medicines are reused.

Figure 3 shows clearly the lower cost achieved by reusing some medicines. Specifically in this case, a waiting time of 23 minutes can be achieved at a cost of €70 per day. This is €35 cheaper than the case where no medicines are reused.

6 Discussion

Initially this system at NKI-AVL was analyzed with a simulation model. This approach was chosen due to the multiple time scales (which typically makes analytic analysis difficult) and because hospital staff were more familiar with this approach. However when the
case study component of this work was completed and it became apparent that improvements would be realized, we sought to formulate an analytical solution which would be easily reproduced in other settings or when prices of medicines changed. As such, other hospitals with similar practice as the NKI-AVL can use the same methods to determine the waiting times of the patients and the cost to the pharmacy.

In case no medicines are made in advance, equation (4) gives an approximation of the waiting times. If a hospital has a policy of making multiple medicines in advance, equation (5) should be used. Equation (7) gives the cost to the pharmacy for each policy. The plots in Figures 2 and 3 can easily be reproduced in other hospitals to illustrate the costs and waiting times associated with various policies $M$ and $F$ (and likewise for the current policy). This approach leaves the decision autonomy with the hospital managers, allowing them to decide how the waiting times of the patients and the cost of the pharmacy should be balanced, (i.e. which metric should be given more weight).

The interactive nature of the two departments in this study is a prime area for further study. The two departments have different and sometimes competing objectives and models such as the one presented in this paper are needed to quantify the concerns of both. As shown, significant improvements in patient waiting times can be gained at a low cost for the hospital.

A topic for future research would be to examine possible implications of our research for the appointment scheduling at the CDU. In this paper we considered the appointment schedule as given. However one can imagine that changes in the appointment schedule will affect the workload at the pharmacy. On the other side the pharmacy could develop a medicine preparation policy based on the appointment times of the patients at the CDU, for instance, making medicines in advance only for patients that are scheduled in the morning.

In this paper policy $M$ is defined such that once we indicate that a medicine is to be made in advance, all orders for this medicine are made in advance. It is likely that further improvements are possible if we relax this restriction and further specify this policy. For example we could choose which orders to make in advance based on all outstanding orders by taking the length of the queue into account. This more complicated situation would
better reflect the current state of the system, however it would likely require a model in real time. How to incorporate a “real time” policy into current practice, and examining if the gains justified the more complex policy, are additional areas for further research.

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References


