PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE
ESCUELA DE INGENIERÍA

APPOINTMENT SCHEDULING AND PATIENT PROGRAMMING IN CHEMOTHERAPY: A CASE STUDY IN A CHILEAN HOSPITAL

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Tesis para optar al grado de
Magíster en Ciencias de la Ingeniería

Profesor Supervisor:
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Santiago de Chile, Noviembre, 2016

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Todo lo que somos es el resultado de
lo que hemos pensado; está fundado
en nuestros pensamientos y está
hecho de nuestros pensamientos.

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RESUMEN

Esta investigación aborda un problema real de agendamiento para pacientes de quimioterapia en el Hospital del Salvador en Santiago de Chile. El problema presentado puede dividirse en subproblemas. El primero corresponde a la forma de asignar las sesiones de los pacientes en el tiempo y el segundo tiene relación con el funcionamiento diario de la unidad de Quimioterapia, cómo son establecidos los horarios de atención de los pacientes y cómo se asigna la capacidad disponible (módulos de sillones de tratamiento y horas de atención de enfermeras). Una dimensión adicional del problema que complejiza su solución es la necesidad de contar con horas de laboratorio disponibles para preparar el medicamento de los pacientes debido a que esta capacidad de preparación es limitada. Como resultado se formuló una metodología que aborda el problema en dos etapas. La primera se basa en una investigación previa realizada por Sauré et al. (2012) e implementa para quimioterapia la política de calendarización, sugerida por los autores para la calendarización de tratamientos de radioterapia. El resultado obtenido de esta primera etapa constituye el *input* para la segunda etapa, que consiste en resolver un problema de programación de máquinas en paralelo con restricciones adicionales de capacidad. Esta etapa se aborda mediante la generación de patrones de tratamiento. Se evalúan los beneficios de ambas etapas de la metodología para el caso que enfrenta la unidad de Quimioterapia del Hospital del Salvador. El método propuesto logra reducir en un 20% los costos operacionales del hospital, debido a una reducción en horas extra. Por otro lado, para una demanda promedio el método propuesto para programar pacientes a diario logra aumentar en un 21% el uso de capacidad de atención y en un 22% el uso de capacidad de laboratorio; esto con respecto al método usado actualmente por el hospital.

Palabras Claves: healthcare, scheduling, calendarización de pacientes, programación dinámica, optimización entera.

ABSTRACT

This research addresses a real scheduling problem for chemotherapy patients at the Hospital del Salvador in Santiago de Chile. The problem presented can be divided into two subproblems: scheduling patients on an infinite time horizon and daily patient scheduling. The first one refers to how to allocate treatment sessions in time and the second part is related to the daily operation of the Chemotherapy unit, how daily schedules are established for every patient, and how the available capacity (treatment chairs and hours of nursing care) is allocated. We consider the requirement for available lab hours to prepare the medicine for every patient as an additional complexity. As a result, a methodology was formulated that addresses the problem in two stages. The first one is based on previous research conducted by Sauré et al. (2012), which implements the scheduling policy for chemotherapy, suggested by authors for radiotherapy treatments. The result of this first stage is input for the second stage, which consists in solving a problem of parallel machine programming with additional capacity constraints. This stage is addressed by generating treatment patterns. The benefits of both stages, of the proposed methodology are evaluated for a real case in the Chemotherapy Unit in Hospital del Salvador. Regarding the costs' impact, the method proposed manages to reduce in a 20% the operational costs of the hospital, due to less extra treatment hours needed. On the other hand, the proposed daily scheduling method for patients presents an improvement of 21% in care slots usage and 22% in lab slots usage for an average demand day with respect to the current methods applied to the use of resources. This translates in a reduction of both extra hours used and workday duration.

Keywords: healthcare, scheduling, patient scheduling, dynamic programming, integer optimization.

1. INTRODUCTION

1.1 Motivation

Within the fields that Operation Research addresses, there is an area focused on the resolution of problems related to scheduling. This consists in allocating resources in a certain time interval, which is subject to specific conditions, in order to satisfy in the best possible way a certain objective (Wren, 1996). The scheduling problems are frequently present in the area of health, where they have been approached from different perspectives: to schedule medical staff shifts (Burke et al., 2004); to allocate hours for the use of scarce resources, such as operating rooms or laboratories; and to schedule appointments of health care to patients (Cayirli and Veral, 2003). Within this last category, there is a specific problem of scheduling appointments for medical treatments, such as dialysis, chemotherapy, or physiotherapy.

1.2 Problem Description

1.2.1 Chemotherapy Context

The problem that this investigation addresses is the one faced today by the Unit of Chemotherapy of the Salvador Hospital, in Santiago of Chile. According to the American National Cancer Institute, chemotherapy is a type of cancer treatment that uses pharmaceuticals in order to destroy cancer cells. This treatment can be prescribed to a patient for two reasons: to cure cancer (healing), or to relieve the disease symptoms (palliative). This type of treatment consists of several sessions of varying duration, which can be accompanied by other treatments, such as radiotherapy or surgery.

There is a medical team that determines the treatment for each patient, based on the type of cancer the patient presents and the severity in which it is found. If a patient has possibilities for improvement, a healing treatment will be prescribed, which includes chemotherapy, radiotherapy, surgery, or a combination of these. On the other hand, if a patient does not have any chance of recovery, a palliative treatment will be prescribed, in which pharmaceuticals will be provided in order to relieve the patient's symptoms. Also, a patient who has not evolved successfully during its healing treatment falls in this category.

1.2.2 Structure and Complexity of the Problem

The scheduling of chemotherapy patients may consider two dimensions: the scheduling of sessions in an infinite horizon of time, and the daily scheduling of patient care. Each of these dimensions presents several challenges from the operational viewpoint.

Concerning the first dimension, it is required that the sessions follow the predetermined structure, for the treatment to be effective. Hence, once the appointment is scheduled, it is not possible to change it in case there is no medical capacity to treat the patient. This implies that it is possible that there is no allocation of patients, whose treatments fit perfectly and no modules are lost (Sauré et al., 2012). Furthermore, there are some types of cancer with a higher priority care than others, whether for urgency, speed of disease development, or for improvement possibility. Therefore, it is not possible to schedule patients under a First In First Served policy.

The second dimension, which is related to daily chemotherapy patients' care, presents two great challenges. Firstly, each chemotherapy treatment uses a determined quantity of limited resources: hours spend in a treatment chair, considering both oncologists and nurses. In this vein, an important aspect to consider is the impact of the laboratories operations in the daily management of chemotherapy patients. In the case of the Salvador Hospital, the Unit of Chemotherapy works directly with Central Mixing, the laboratory in charge of preparing the necessary pharmaceuticals to treat the patients. This laboratory has limited time capacity, aimed to prepare the hospital's orders, which constrains how patients should be managed on a daily basis. On the other hand, chemotherapy treatments state that certain pharmaceuticals can be prepared beforehand (usually the day before treating a patient), and others must be prepared the very same day in the morning. Therefore, there is a limitation that requires treating certain patients from a specific time onwards, which increases the complexity of the problem.

The second challenge is the complexity of the problem structure itself. The daily scheduling of patients is categorized as a problem of parallel machine programming, where each treatment chair corresponds to a machine, and the patients' sessions to tasks that must be assigned to each chair. This problem is NP-complete (Du and Leung, 1990), and must be solved for numerous parallel machines, which implies an extensive associated combinatorial, and therefore, requires a different approach from the classical mathematical modelling.

1.3 Relevance of the Problem

Nowadays, the methodology used by the Unit of Chemotherapy, in order to schedule the patients and schedule daily treatment sessions, consists in the use of extra hours of care, and postponing the initiation of certain patients' treatment. This is due not only to the lack of care capacity (both in medical hours and treatment modules), but also it is the outcome of an unplanned management of care hours, nurses shifts and treatment chair hours. The costs of not having a proper scheduling of patients is monetary, as it implies and extra expense for the hospital to supplement the lack of capacity with extra hours; as well as social, as certain patients have to delay their treatment initiation due to the lack of capacity, which decreases their chances of recovery (Ragaz et al. 2004).

There are publications available in literature, which state that a delay in the treatment initiation of a patient has detrimental effects in their chances of survival, either because there is a progress in the development of the tumours, or because the symptoms worsen rapidly over time. This happens, for example, in patients with testicular or colon cancer, where both diseases are quite frequent, and develop rapidly over time (O'Rourke and Edwards, 2000; Chen et al., 2008; Sauré et al., 2012; Song et al., 2013; McLaughlin et al., 2012; Bos et al., 2015; Bernard and Sweeney, 2015). Therefore, relying on a formal, efficient, and robust methodology that allows the scheduling of patients and plan the daily health care is essential in order to decrease the extra expense of the Unit of Chemotherapy.

1.4 Objectives

1.4.1 Main Objective

The main objective of this research is to develop a methodology to address patient scheduling and programming. This methodology will support decisions related to the allocation of resources in the Healthcare area, more specifically in the Chemotherapy Unit of a public hospital.

1.4.2 Secondary Objectives

a) Understand the current operation carried out in the Chemotherapy Unit, identify critical processes that require improvement and define indicators to evaluate system performance.

b) Develop a methodology based on Dynamic Programming and Mathematical Integer Programming to improve scheduling of chemotherapy treatments and patients' daily programming.

c) Compare the results obtained from the proposed methodology with those presented by the methodology currently used by the hospital, through the previously defined performance indicators.

1.5 Hypothesis

By implementing a methodology for patients' scheduling and daily programming it is possible to reduce operational costs related to extra hours for medical consultation and treatment and achieve a better management of the resources available (care hours, nurses and treatment chairs) in the Chemotherapy Unit of the Salvador Hospital. Also, since chemotherapy treatments require a strict compliance of treatment cycles and sessions, we expect to achieve regularity for every patient by incorporating uncertainty to patient's demand and scheduling process. Finally, with the methodology proposed we seek to reduce extra working hours and the total length of a workday by programming patients more efficiently through Operations Research tools.

1.6 Existing Methodologies

This research focuses on the scheduling of chemotherapy treatments and addresses two main issues: the scheduling of patients through time and the daily scheduling of these patients' care services. The first issue refers to the allocation of medical hours or treatment sessions in a time horizon. Within the available techniques to solve scheduling problems, dynamic scheduling considers variables that are subject to random events and it has been used to address problems not only in healthcare. For example, it has been used in the industrial sector to solve staff planning problems, specifically the scheduling of working shifts that consider days off, part-time workers, absenteeism, among others (Ernst et al. 2004); and in the airline industry to determine commercial flights itineraries (dates, boarding gates, and port of landing) (Warburg et al. 2008, Jiang and Barnhart, 2009).

In healthcare, this method has been used to coordinate the daily allocation of medical resources (medical and nursing care) to patients in a clinic (Gupta and Denton, 2008), to schedule medical care and treatments for patients with different care priorities (Patrick et al., 2008, Sauré et al., 2012) and to schedule patients considering no-show (Liu et al., 2010).

The second issue that this research approaches refers to the scheduling of the daily functioning of the chemotherapy unit. This problem can be formulated as a machine programming model which can be divided into different categories: machines in series or in parallel, independent or dependent on each other, uniform or different processing times on each machine, among others (Graham et al., 1979). The daily problem that the hospital has to solve corresponds to a machine programming problem with parallel machines, dependent on each other, where the objective is to minimize the moment in which the last patient ends its treatment.

Among the existing works we can mention Yalaoui and Chu (2001), who solved the machine-programming problem in parallel through a Branch and Bound algorithm, Anghinolfi and Paolucci (2006) who present a hybrid metaheuristic which combines Tabu Search and Simulated Annealing in order to achieve an approximation to the solution of the problem, and Li et al. (2011), who suggest different theoretical approaches to the solution and a heuristic of resolution based on Simulated Annealing. Other authors that suggest the implementation of heuristics in order to solve the machine-programming problem are Bilge et al. (2002), who present a heuristic based on Tabu Search.

Between the publications available in literature, it was not possible to find any in which the programming of machines model was used in order to solve the scheduling of patients problem. However, there are publications that try to solve this problem (or variations of it) through other approaches. Among the works that are closer to solve the problem that this research addresses we could mention Conforti et al. (2008) and Condotta et al. (2014). The first ones present the daily scheduling problem of radiotherapy patients, and propose an optimization model that maximizes the number of treated patients. The second authors mentioned solve both the scheduling of patients through time problem and the daily scheduling of patients' care services.

The scheduling problem of treatments has been approached in literature considering diverse features, such as session length, if multiple types of priority or capacity requirements for patients are included or if the use of overtime is allowed or the horizon of scheduling is finite or infinite (Patrick et al., 2008; Conforti et al., 2008; Conforti et al., 2010; Sauré et al., 2012.; Condotta and Shakhlevich, 2014). Concerning the configuration for medical treatments, Cayirli and Veral (2003) perform a categorization of the types of treatments in healthcare (individual block of fixed length, variable length, multiple blocks, etc.).

Literature referring to the scheduling of cancer treatments (both chemotherapy and radiotherapy) is divided into two currents of thought: one that approaches the problem in a static manner and another one that solves the problem in a dynamic manner. In the static problem, the scheduling choices are made at the beginning of the evaluation period. On the other hand, the dynamic refers to the methods used for scheduling appointments for patients before they set a day for their treatments, when the demand is yet uncertain.

Among the publications that address the scheduling problem in a static manner, the work of Conforti et al. (2008) can be found, who propose a mathematical model to solve a radiotherapy session scheduling problem. Petrovic and Leite-Rocha (2008) address the radiotherapy-scheduling problem as well, and they consider two rules for scheduling: forward and backward. The former refers to begin scheduling patients from their waiting deadlines, while the latter refers to scheduling patients as they enter the system. This research aims to establish rules or policies that enable scheduling in an easy and rapid manner, without impairing the quality of the solution. Among recent publications that aim for this type of perspective, Patrick et al. (2008) and Sauré et al. (2012) can me mentioned, who pose scheduling policies under a dynamic approach. Both publications consider an infinite horizon of time, multiple priorities, and the use of overtime.

The scheduling of chemotherapy treatments may address not only the scheduling of sessions, but also the manner in which these patients must be treated daily. A work already available in literature, which considers both stages, is the Condotta and Shakhlevick's (2014) one. They not only schedule patients in a finite horizon of time, but they also determine the sequence of activities for the personnel during the day. However, unlike our research, the authors consider a static approach for scheduling the patients' sessions, and they do not include in the daily timetabling the use of laboratory capacity for the medication preparation.

In the same vein of daily patient scheduling, the work of Le et al. (2015) can be mentioned, who solve the scheduling problem of hematology and chemotherapy treatments. For this, the authors propose a mathematical model first and a Tabu Search heuristic in a second stage. The problem solved by the authors considers a static scheduling, in which the treatment sessions of the patients are allocated together, disregarding the uncertain future demand. On the other hand, the problem solved by Let et al. (2015) aims to optimize the allocation of the nurses' workload, and disregards the required time for the medication preparation for the patients, two issues that differ from the approach proposed in this research.

1.7 Research Contribution

The objective of this research is to develop a methodology for patients scheduling and programming in a Chemotherapy Unit. The problem we approach can be divided in two stages: scheduling patients in a time horizon and programming patients' daily attention. We consider an infinite horizon of time, stochastic demand, arrival times and capacity requirements for each patient, the structure of every treatment (cycle time and number of sessions) and lab capacity for drug preparation. To our knowledge, there is not a research on literature that has addressed both problems (scheduling and daily programming) together with additional lab restrictions and a stochastic demand. It is important to highlight that the proposed methodology will be contrasted with the performance of the methodology currently used in the Chemotherapy Unit of Salvador Hospital to demonstrate the applications of the method we propose to a real problem. We also hope that this methodology can be implemented in other public health centers in the country.

1.8 Problem Definition

1.8.1 Characterization of Chemotherapy Treatments

A chemotherapy treatment is composed by a determined amount of sessions, in which the patient is provided with a specific combination of medication. These sessions have a defined length, which may vary according to the treatment or even for a same treatment, and are held throughout a time horizon according to a cycle that could be every month or every two weeks, for example. The established structure for the treatment should be respected in order for the treatment to be effective, therefore, it is not possible to reschedule sessions if there is no capacity for a certain day.

Figure 1 provides two examples, where each number within the table indicates the amount of time slots needed for a session in the appointed day. We determined based on the diverse existing treatments that the minimum duration unit for a treatment is 15 minutes, so each time slot corresponds to a 15 minutes block. The first case (colorectal cancer) has a cycle every two weeks, in which the patient is provided a session of 3 hours and 45 minutes that should be repeated twelve times in order to complete the treatment. In the second case (esophageal cancer) the treatment is monthly, and the patient must be provided 4 consecutive sessions of varying length, scheme that should be repeated twice.

Colorectal cancer: 12 cycles, cycle: 15 days

	mon	tue	wed	thu	fri
week 1	**15**	0	0	0	0
week 2	0	0	0	0	0
week 3	**15**	0	0	0	0
week 4	0	0	0	0	0

Esophageal cancer: 2 cycles, cycle: monthly

	mon	tue	wed	thu	fri
week 1	**13**	**27**	**27**	**27**	0
week 2	0	0	0	0	0
week 3	0	0	0	0	0
week 4	0	0	0	0	0

Figure 1: Graphic representation of the cycle structure of two different chemotherapy treatments

For each session (or set of sessions corresponding to one week) the patient must be treated firstly with the treating oncologist, who requests for an examination in order to validate that the patient is in condition to receive a treatment. Therefore, every time a cycle begins an hour for medical consultation is also needed, which fluctuates between 15 and 45 minutes. This consultation can only be held within the same week in which the patient will be treated, because if there were a longer time separation, the patient's examination would no longer be valid. Finally, each session needs a determined amount of lab slots in order to prepare the medication, which requires in certain cases to be prepared the very same day.

1.8.2 Available Resources

The Chemotherapy Unit is composed by one oncologist, three clinical nurses who are in charge of executing the treatments, and seven treatment chairs. The oncologist works twice a week, has a care capacity of 36 slots of 15 minutes each, and the average length of a consultation corresponds to two slots (30 minutes). On the other hand, each clinical nurse and treatment chair is available for 36 slots every day. The lab receives preparation orders for a certain day until the previous day at midday. It also dedicates a number of time slots in the morning to prepare the medication that requires to be made the very same day.

1.8.3 Patient Scheduling Throughout a Time Horizon

Patients arrive randomly to the Chemotherapy Unit, where they are evaluated by a group of oncologists who determine the type of chemotherapy treatment each patient has to undergo. Every patient has to go through a previous process in order to start its treatment, which may take one or several sessions with the treating oncologist. This research will not include this stage, and the entry day of a patient to the system will be considered as the day in which all the previous stages of treatment approval are already done.

Since the treatments have a fixed structure that indicates the amount of sessions and the gap between them, the decision is when does each patient start its treatment and it depends on the available capacity of i) time slots for patient care (medical attention) and ii) time slots for patient care in every treatment chair. Patient scheduling is done from one week to another, that is to say, every week patients are admitted and scheduled at the end of that same week for future days.

It is noteworthy that for every type of cancer there is a maximum time stipulated to postpone the start of a patient's treatment, due to the rapid development of cancer. Furthermore, every type of cancer has a priority level assigned under medical criteria, which considers factors such as the severity of the disease, improvement probabilities, and additional constraints established by the Ministry of Health. Therefore, the timetabling must respect this prioritization when allocating patients throughout the time horizon.

Example 1. Consider a small example of 10 patients arriving to the system throughout one month. In Figure 2 two timetables can be observed, where the upper one corresponds to the patient care scheduling (oncologist session), and the lower one to the treatment sessions. Each row corresponds to the timetable of one patient, and the hatched area indicates weekend days in which there is no patient care. The arrival day of each patient to the system is known (red blocks), and based on this information a medical appointment is scheduled with the treating oncologist, starting from the week after its entry (see upper timetable). There are cases in which the patient may be delayed beyond the week after its entry, such as the case of patients P2 and P8. Patient P2 enters during the first week, however, its first session is scheduled for the third week. Likewise, patient P8 enters the third week, but the start of its treatment is postponed at least two weeks. These delays are due to the non-existing capacity of patient care for a consultation to take place prior to the session the week after the patient's entry. It can be observed that the lower timetable structure, corresponding to the treatment sessions, depends on the scheduling with the oncologist. As a general rule, the consultation with the treating oncologist must take place the same week of the treatment sessions. Nonetheless, there are some treatment schemes (as the colon cancer one) that require five consecutive sessions. Therefore, an exception has to be made for these cases, and the consultation takes place the previous week, as late as possible.

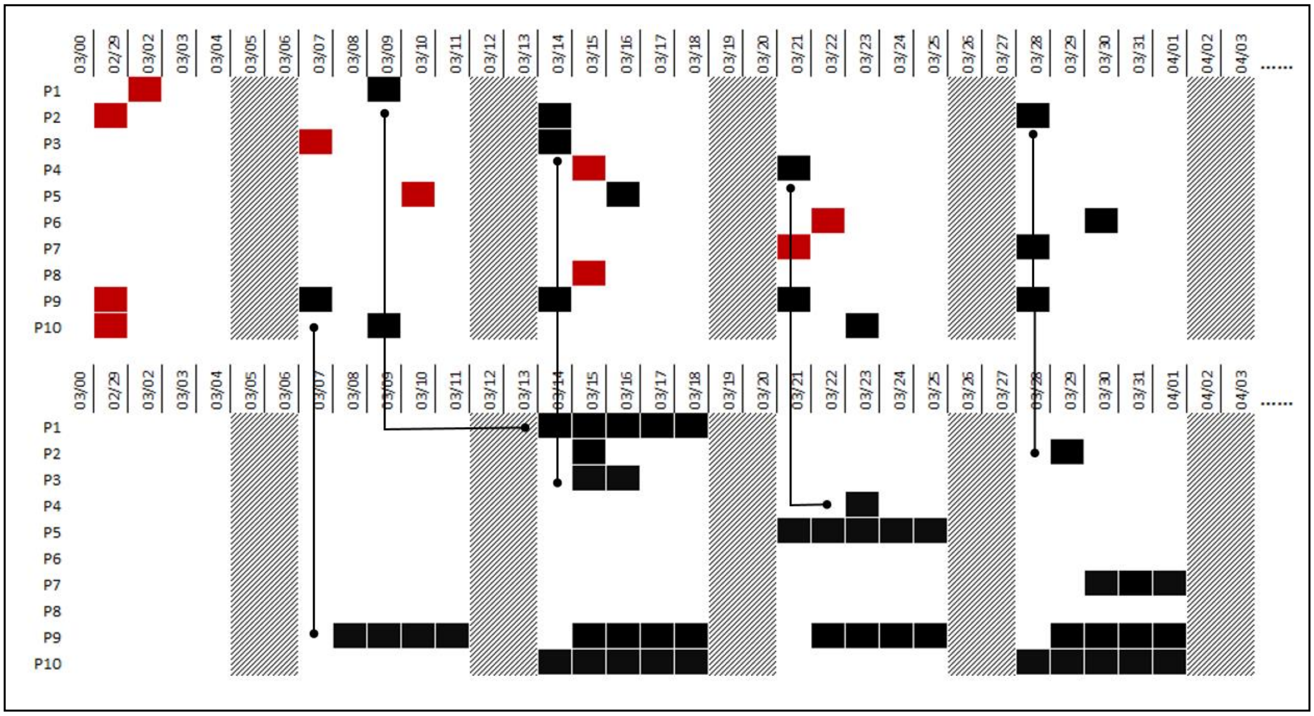

Figure 2: Example of the arrival and scheduling of medical appointments of patients for a month of the time horizon

In order to measure the impact of the scheduling decisions, three metric units were established: Delayed Patients Percentage (DPP), Extra Consultation Slots (ECS), and Extra Treatment Slots (ETS). The first two metrics are related to the service given to the patients with respect to the waiting in order to begin their treatment, and to the saturation level of the system, because the constant delaying of the patients indicates there is a lack of patient care capacity. The third metric allows the quantification of the missing capacity and identifying if the scarce resource is the amount of medical hours or treatment hours. The final result of this first stage is the allocation of patients to their first day of treatment, and therefore, since there is a specific protocol for every patient that defines the treatment structure, the complete agenda of the sessions for each patient is determined. It is possible to build the whole calendar with this information, and determine for each day which patients must be treated.

1.8.4 Daily Patient Scheduling

The procedure used by the hospital in order to achieve a daily planning begins with deciding which patients and when will they be treated in each of the treatment chairs. Once this allocation has been done, there is a list of chores per chair, determined by the treatments of the corresponding patients. This list of chores is assigned to the clinical nurses, which results in a sequence of daily chores for every nurse. It is noteworthy that, as a general rule, if a nurse starts treating a patient, it must perform all the stages of the treatment that correspond to that patient. However, in the case of the hospital where this research was conducted, it is allowed for a patient to be treated for more than one nurse. Therefore, it is necessary that at least one of the nurses is available in order to start a treatment, and that this or other nurse is available to finish it.

A further significant condition that is considered in this research is the laboratory service capacity. The preparation of medication is done by only one chemist in an external lab, who receives preparation orders in determined hours, and dedicates a limited time to prepare these orders. The lab can prepare the medication of one day the day before since midday henceforth, or the very same day in the morning. Also, certain slots of the previous day in the morning could be used, if they are available and there is lack of capacity. In case all the available capacity of the lab is used (capacity given by the chemist availability), the preparation of the medication will be externalized to another lab, which implies an additional cost for the hospital.

Example 2. Figure 3 shows a scheduling of patients for a random day in Chemotherapy. The patients that should be scheduled and number of slots required is known information, as well as those whose medication must be prepared for that same day. The preparation time for medication fluctuates between 30 minutes to 2 hours. Diagram a) shows a timetable for 13 patients, of whom only two (P3 and P10) require their medication prepared the same day. For this example, 3 clinical nurses were considered, and the slots in which the resource nurse is used at full capacity can be observed in the diagram. The hatched area corresponds to the patient care time that was not used. Given the characteristics of the treatments and the restriction of not exceeding a maximum of nurses, it is not possible to distribute the patients in a way that they fit perfectly and no slots are lost during the day. Diagram b) shows the lab hours used the day before (left scheduling) and for the same day (right scheduling) of these same patients. The example considers for day *n* a lab capacity of 2 hours (8 slots) in the morning of the *n* and *n-1* days, and 4 hours in the afternoon (16 slots) for day *n-1*. It is possible to see that all the lab slots of both mornings are completely used, and that day n-1 in the afternoon is collapsed, which implies externalizing the medication preparation to another lab for patients P12, P26 and P11. Furthermore, it is possible to see, in case there is available capacity in the morning of day n, that it is not possible to reschedule any patient (in this case, P6 and P26 cannot be treated the day before, because there would not be time to prepare their medication), which reflects that deciding at which time to schedule each patient, regarding the lab restrictions, is not trivial.

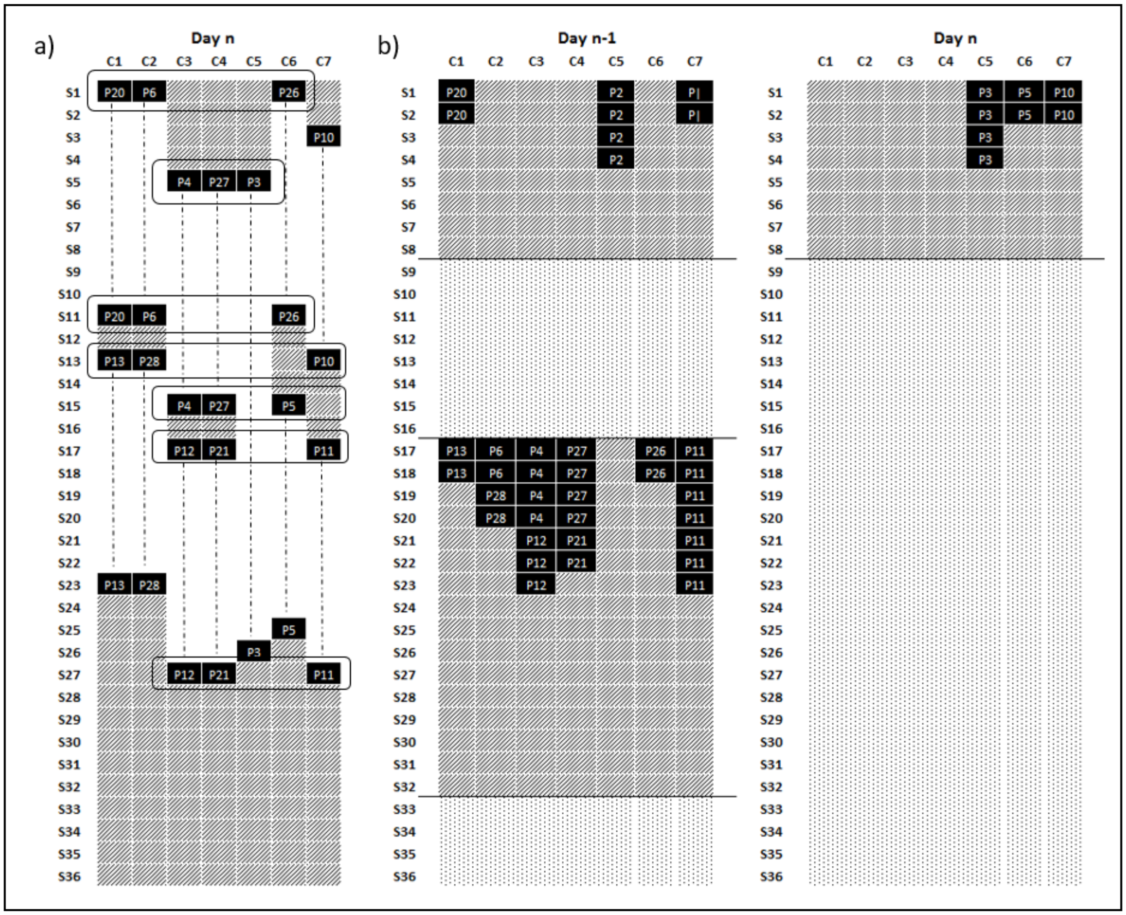

Figure 3: Example of patient scheduling for any day of 36 time slots (from 8 AM to 5 PM)

In order to measure the impact of the proposed method to schedule patients and compare it with the one used by the hospital nowadays, two metric unites were determined: finishing time of the last patient (FTLP), and extra slots used in order to treat the patients (EST). The former is related to the number of extra hours incurred by the Chemotherapy Unit, while the latter indicates the amount of extra capacity (in care slots) needed so extra hours are not required. It is important to note that it is possible to increase the care capacity not only by increasing the amount of daily worked hours or treatment chairs, but also increasing the lab availability.

1.9 Solution Approach

1.9.1 Dynamic Patient Scheduling

In order to schedule the patients throughout a time horizon and determining the days in which they have to attend to a session, we implemented the model posed by Sauré et al. (2012). This method solves a scheduling problem of radiotherapy patients through the formulation of a Markovian Decision Process, which considers an infinite time horizon, multiple appointments, sessions of diverse lengths, and the use of overtime.

The methodology the authors propose aims to minimize three components: cost of starting a treatment a certain day, cost of overtime usage, and cost of delaying the scheduling of a certain type of treatment. The method allowed the identification of the following scheduling policies for radiotherapy treatments:

- Schedule the greatest amount of demand the first day available, and the rest starting since their deadlines for beginning their treatments.
- The greater the number of sessions, the treatment should be scheduled earlier.
- Those treatments with shorter sessions should be scheduled further in the future.
- The more urgent treatments, or with fewer time allowed to begin, should be scheduled as soon as possible.

Since radiotherapy and chemotherapy treatments consider in their structures the same conditions (in fact, radiotherapy treatments are a particular case of chemotherapy), the arrival of patients to the system in both cases behaves according to a Poisson distribution, and since Salvador Hospital considers the same costs to decide how to schedule the patients, it is possible to adapt the policy posed by Sauré et al. (2012) to chemotherapy treatments.

In order to implement the scheduling policy, it is necessary to define a category for the diverse treatments that the hospital currently has. This categorization is done based on the similarities of treatment structures, which include the amount of slots, cycle length, number of sessions and their durations. Once the treatments are grouped by type, two parameters must be established: booking horizon, which corresponds to the time horizon in which patients will be scheduled; and planning horizon, which corresponds to the whole time horizon in which patients will be scheduled. The planning horizon should consider at least the number of days as the booking horizon, plus the days of the longest treatment.

This scheduling policy differs from the one currently used by the hospital, since the latter conducts a short sighted allocation. That is to say, the medical appointments are scheduled according to patient arrival and no further capacity is booked in advance. However, it is important to highlight that in both cases there is a prioritization of patients, but in the hospital's case this is only based on medical criteria (urgency and improvement possibility). When implementing this scheduling policy, two calendars are obtained. One contains the days when each patient must attend to a medical appointment, and the other one indicates which days correspond to a session. This information is an input for the second stage of this methodology.

1.9.2 Pattern Generation for the Daily Scheduling of Patients

The daily scheduling of patients consists in determining a care order for a list of patients who have to be treated on the same day. This care order indicates in which treatment chair each patient has to receive its treatment and in which time slot. Therefore, for each chair a sequence of patients, who have to undergo chemotherapy sessions of varying length and different medical requirements, is determined. Treatment chairs work in parallel, so it is possible for several patients to be treated simultaneously, as far as there are available nurses. Finally, every treatment session specifies a time for the preparation of medication that could be produced the day before the patient's session or the same day in the morning. This time determines the possible time slots for a patient to start its treatment.

The decisions that have to be made present a challenge from the computational capacity viewpoint that is needed in order to solve the problem to optimality. In Example 2, which considers 7 treatment chairs, 14 patients during the day and 36 slots, the number of variables that indicate the allocation of patients, as well as the sequence in which they should be treated, is 9,359, and the number of corresponding restrictions is close to 78,403. An example of this dimension could be solved in a considerable time (more than one day) if there was a significant computational capacity, which is not applicable to the hospital's situation, as they have to solve this problem on a daily basis. Given the complexity of the problem structure, which presents a combinatorial that rapidly grows if more patients, chairs, or slots are considered, it is necessary to propose a new methodology to solve the problem.

We define treatment patterns in order to address the problem. A pattern corresponds to a possible allocation of patients to any chair, in which the sequence of patients and the slot in which they will start their treatments is indicated. To construct the patterns it is necessary to know what patients will be treated that day and how many slots their respective sessions require; information that is already known since it is the result of solving the previous scheduling problem. Then, it is possible to determine all the feasible combinations (or groups) of patients for one treatment chair, which works a certain amount of slots per day (see Table 1). Once the feasible combinations for patients who can be allocated to one treatment chair have been determined, treatment patterns are generated on this basis. For each combination of patients there are multiple possibilities to place them in sequence.

Table 1: Generation of some feasible combinations on the basis of 15 patients for one treatment chair that works for 36 slots (9 hours), daily

Pacient	*Session duration (15 min slots)*
P1	10
P2	10
P3	5
P4	11
P7	25
P9	10
P10	10
P11	10
P14	5
P15	11

Some feasible combinations:	*Patients*	*Total slots*
combination 1:	P1, P2, P3	25
combination 2:	P9, P10, P11, P14	35
combination 3:	P12	22
combination 4:	P5, P6	34
combination 5:	P13, P14	9
combination 6:	P3, P8, P13, P14	16
combination 7:	P7, P8	27
combination 8:	P9, P10, P11	30
combination 9:	P12, P4, P8	35
combination 10:	none	0

Example 3. Figure 4 shows 10 possible patterns for the combination P1, P2, P3. Every pattern indicates both the order in which the patients will be treated, and the slot in which each one begins its treatment. It is noteworthy that since each patient may start its

treatment in different slots, the number of feasible permutations for each combination of patterns increases rapidly. For this example that considers only one combination (P1, P2 and P3), the amount of possible patterns is 20,956. If the example is considered for a day shown in Table 1, where there are 10 combinations, the amount of patterns for one day reaches 2,170,723. Therefore, for an example with a greater amount of combinations, the number of possible permutations easily reaches the million scale.

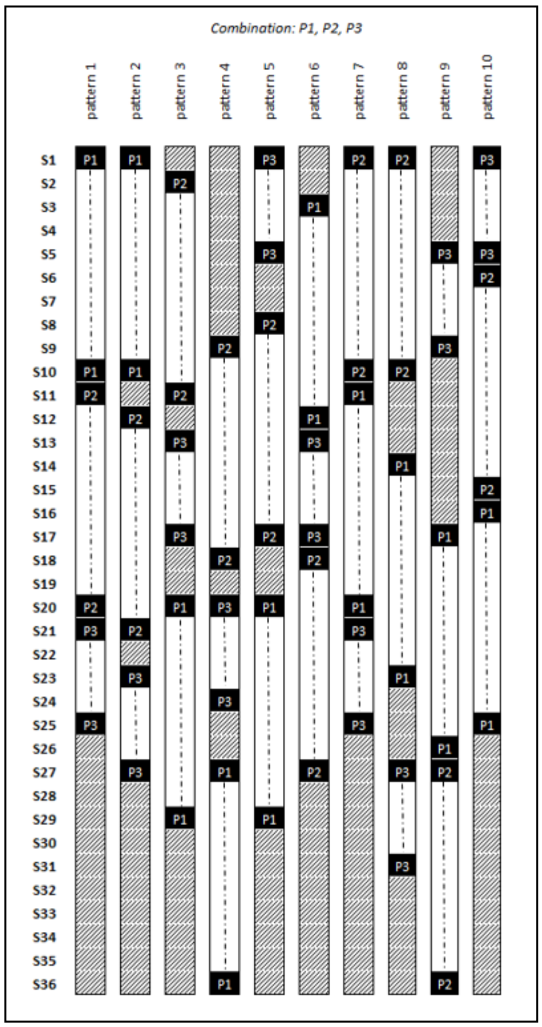

Figure 4: Possible patterns for the combination of patients P1, P2, P3.
The hatched area corresponds to unused slots. P1 and P2 use 10 treatment slots, while P3 uses 5 slots.

1.9.3 Optimization Model for the Daily Scheduling of Patients

This problem considers a set of patients J who should be treated on day t. Each day is divided into a number of 15 minutes slots contained in set M. For every day there is a set of patterns P, which contains all the feasible allocation patterns for day t. Finally, sets S and T correspond to the amount of treatment chairs at disposal and the number of periods (days) for which a scheduling is required. In order to obtain the solution for a specific day, it is necessary to consider at least two periods of time, because while the patient care is during day t, there are lab slots of day t-1 in which the medication for day t might be prepared.

To consider the resources of the Chemotherapy Unit, the following parameters are defined:

- NE corresponds to the number of nurses available for patient care.
- $\beta_{t,m}$ is the binary parameter that equals 1 if the laboratory is busy during period t and slot m, and 0 otherwise.
- QL_j indicates for every patient j how many lab slots are required to prepare the medication needed (information established in the corresponding treatment protocol).
- α_j binary pattern that equals 1 if the medication of patient j has to be prepared the same day, and 0 otherwise.

Finally, to integrate the information of the patterns generated in a previous stage, the following parameters are defined:

- $A_{p,j}$ equals 1 if pattern p contains patient j.
- $I_{p,m}$ equals 1 if pattern p contains slot m as a start. A pattern includes one or more patients, all of them with different starting slots. Therefore, this parameter equals 1 as many times as there are patients contained in the pattern.
- $II_{j,p,m}$ equals 1 if given a patient j in particular, any pattern p contains that patient j, and also this patient begins its treatment in slot m.
- $F_{p,m}$ equals 1 if pattern p contains slot m as an ending. Under the same concept as parameter $I_{p,m}$, this parameter will equal 1 as many times as patients are in pattern p.
- H_p corresponds to the amount of extra hours associated with pattern p. In order to determine the value of this parameter, the difference between the finishing time of the last patient (according to what the pattern indicates) and the slot in which the working hours should finish has to be calculated. To consider extra hours in the modeling, the criteria by which patients are selected for a combination (see Table 1) must be modified, adding the extra hours to the whole duration of a workday.

Since treatment patterns contain the feasible sequence information in which a patient could be allocated to a chair, the problem is simplified to one of pattern allocation to treatment chairs. Nonetheless, it is also necessary to incorporate the lab dimension to the model, for which the following variables of binary decisions are defined:

- $x_{p,s,t}$ = equals 1 if pattern *p* is assigned to chair *s* on day *t*.
- $y_{j,m,t}$ = equals 1 if the patient *j*'s medication is prepared during slot *m* on day *t*. The preparation of a medication may last longer than one slot. In this case, once the chemist starts to prepare it, it does not stop until it is finished. Thus, this variable will equal 1 for a same patient, for a certain amount of consecutive slots, so as to assign the necessary amount of preparation slots.

By using patterns the restrictions of a sequencing and allocation model are reduced to two. The first one corresponds to the allocation of every patient to a treatment chair (see Eq. 1); the second one, ensures that every chair has just one pattern associated to it, since each pattern describes the complete sequence of care, for a day, for any chair (see Eq. 2). Finally, because patients are treated in chairs that work in parallel, and since there is a fixed amount of nurses, we must consider the restriction stipulating that in every moment of time the amount of patients requiring care cannot exceed the total amount of nurses NE (see Eq. 3). The moments in which a patient requires care are when they begin their treatment and when it finishes. During the process it is assumed that the patient is sit in a treatment chair and there is no nurse care required.

$$Eq.1: \sum_{s\epsilon S} \sum_{p\epsilon P:\, A_{p,j}=1} x_{p,s,t} = 1 \qquad \forall\, j\epsilon\, J, t\,\epsilon\, T$$

$$Eq.2: \sum_{p\in P} x_{p,s,t} \leq 1 \qquad \forall\, s\,\epsilon\, S, t\,\epsilon\, T$$

$$Eq.3: \sum_{s\epsilon S} \sum_{\substack{p\epsilon P: \\ (I_{p,m}=1 \text{ or } F_{p,m}=1)}} x_{p,s,t} \leq NE \qquad \forall\, m\,\epsilon\, M, t\,\epsilon\, T$$

To prepare the medication, there are three conditions that constrain the problem, and that determine the sequencing of patients. The first one (see Eq. 4), is to allocate the medication preparation hours of every patient to some of the lab slots available. This restriction does not consider a specific sequence for the modules corresponding to every patient *j*, it just verifies that the total amount of slots required from the lab does not exceed the available capacity of it. The left side of the equation considers possible the medication preparation of a patient the day before (first component of the sum), or the same day (second component of the sum).

The second restriction considered is that all the necessary slots to prepare the medication of patient *j* must be allocated before it starts its treatment (see Eq. 5). This is the condition that relates the lab availability with the allocation of patients to chairs (understanding the allocation as determining a sequence and starting slots), and that constrains the hour in which a patient can start its treatment in case its treatment requires its medication to be prepared the same day. The left side of the restriction ensures that $y_{j,m,t}$ will equal 1 if there is availability of lab, and also if patient *j* has not been allocated to start its treatment before slot *m*. Finally, a restriction is added, which ensures that a medication will not be prepared in two consecutive days (see Eq. 6).

$$Eq.4:\ \sum_{m\epsilon M}(y_{j,m,t-1})(1-\alpha_j)+\sum_{m\epsilon M} y_{j,m,t}=QL_j \qquad \forall\, j\epsilon\, J, t\,\epsilon\, T$$

$$Eq.5:\ (1-\beta_{t,m})(1-\sum_{k:k\leq m} II_{j,p,k}\sum_{s\epsilon S} x_{p,s,t})\leq\ y_{j.m.t} \qquad \forall\, m\,\epsilon\, M, t\,\epsilon\, T, p\,\epsilon\, P, j\,\epsilon\, J\ :\ A_{p,j}=1$$

$$Eq.6:\ y_{j,m,t}\leq 1-\frac{\sum_m y_{j,m,t-1}}{H} \qquad \forall\, m\,\epsilon\, M, j\,\epsilon\, J, t\,\epsilon\, T\ \ and\ H\gg 1$$

Lastly, in order to determine the optimum solution of the problem, an objective function was defined that minimizes the amount of extra hours in which every treatment chair incurs. This ensures that each treatment chair is assigned a pattern that allows the completion of patient care as soon as possible (which is the objective of a traditional machine-programming model). Gathering all the elements, the entire scheduling model obtained is as follows:

$$min \sum_{t \in T} \sum_{s \epsilon S} \sum_{p \epsilon P} H_p x_{p,s,t}$$

$subject\ to:$

$$\sum_{s \epsilon S} \sum_{p \epsilon P:\, A_{p,j}=1} x_{p,s,t} = 1 \qquad \forall j \in J, t \in T$$

$$\sum_{p \in P} x_{p,s,t} \leq 1 \qquad \forall\, s \in S, t \in T$$

$$\sum_{s \epsilon S} \sum_{\substack{p \epsilon P: \\ (I_{p,m}=1\ or\ F_{p,m}=1)}} x_{p,s,t} \leq NE \qquad \forall\, m \in M, t \in T$$

$$\sum_{m \epsilon M} (y_{j,m,t-1})(1-\alpha_j) + \sum_{m \epsilon M} y_{j,m,t} = QL_j \qquad \forall\, j \epsilon J, t \in T$$

$$(1-\beta_{t,m})(1 - \sum_{k:k \leq m} II_{j,p,k} \sum_{s \epsilon S} x_{p,s,t}) \leq \ y_{j,m,t} \quad \forall\, m \in M, t \in T, p \in P, j \in J \ :\ A_{p,j} = 1$$

$$y_{j,m,t} \leq 1 - \frac{\sum_m y_{j,m,t-1}}{M} \qquad \forall\, m \in M, j \in J, t \in T \ \ and\ M \gg 1$$

$$x_{p,s,t} \in \{0{,}1\} \qquad \forall p \in P,\ \ s \in S, t \in T$$

$$y_{j,m,t} \in \{0{,}1\} \qquad \forall j \in J,\ \ m \in M, t \in T$$

1.10 Chemotherapy Unit Context

1.10.1 Patients Demand Profile

The performance of the proposed methodology will be evaluated for the case of an oncology unit, which has a staff of one oncologist, three nurses, and seven treatment chairs. Figure 5 shows the demand distribution for seven months of the medical consultations record, where we can highlight that the 56% of the treated patients, during that period, present colon cancer. In the same vein of Figure 5, Table 2 shows information concerning the entry of new patients to the system. Of the total of patients, the 69% corresponds to new patients (patients who enter the system between January and July, 2015), and this percentage is similarly maintained if the analysis per cancer type is disaggregated. With the information of new patients given by the hospital it is possible to build the rate of entries to the Chemotherapy Unit of new patients per cancer type (see Table 2), data needed in order to implement the posed methodology in previous sections.

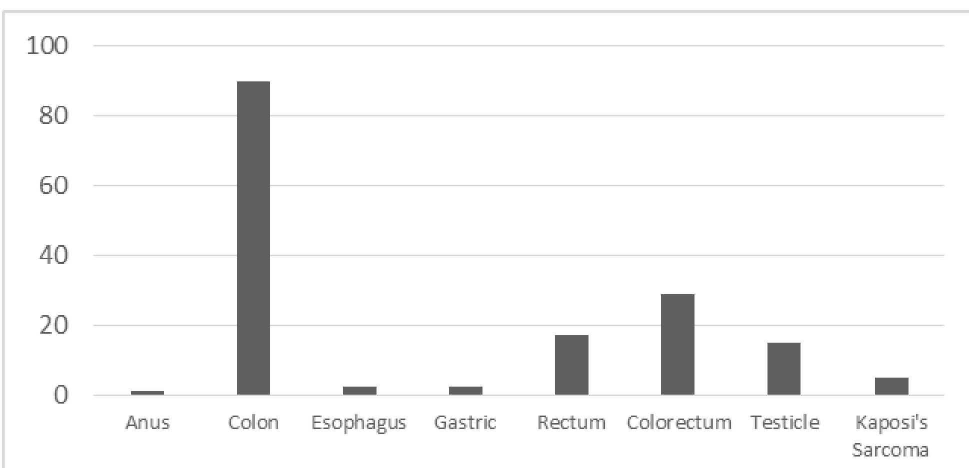

Figure 5: Number of patients per cancer type treated in the Chemotherapy Unit between January and July 2015

Table 2: Characterization of the demand of patients, from the Chemotherapy Unit, treated between January and July 2015

Cancer type	*N° of patients*	*% of total*	*N° of new patients*	*Arrival rate [requests/day]*
Anus	1	0,62%	1	0,005
Colon	90	55,90%	62	0,425
Esophagus	2	1,24%	1	0,009
Gastric	2	1,24%	1	0,009
Rectum	17	10,56%	12	0,080
Colorectum	29	18,01%	20	0,137
Testicle	15	9,32%	10	0,071
Kaposi's Sarcoma	5	3,11%	3	0,024
TOTAL	161	100%	111	0,760

1.10.2 Chemotherapy Treatment Scheduling

Regarding the treatments, there are currently 55 chemotherapy protocols. Among these protocols, 21 correspond to cancer types that have patients' records. In order to group the protocols we categorized them per cancer type and then determined based on the information contained in the protocol, the amount of total slots that each treatment requires and the amount of sessions that a patient must undergo according to the protocol (see Table 3).

Nowadays, the method used by the hospital to schedule the patients is the following. Every week, the medical committee approves the patients who will undergo chemotherapy. Once these patients are ready to start their treatment, they are ordered according to a priority established by medical criteria, and they are scheduled in this order, on Mondays or Wednesdays, depending on the availability of time slots. That is to say, the first patients are allocated on Monday, until there is no more capacity, and then, the scheduling continues on Wednesday. If there is not enough space to allocate the patients, these could be delayed until their deadline, after which they will have to be scheduled in extra hours.

Table 3: Characterization of protocols for chemotherapy treatments for different cancer types

Cancer type	*Treatment description*	*Capacity requirements*	*Sessions/Slots*
Testicle	Protocol 35	3x(5x22)	15/330
	Protocol 36	3x(5x22)	15/330
Colon	Protocol 12	6x(5x11)	30/330
Colorectal	Protocol 11	4x25	4/100
	Protocol 26	12x15	12/180
	Protocol 37	8x12	8/96
	Protocol 39	8x12	8/96
Rectal	Protocol 38	1x1	1/1
Gastric	Protocol 15	4x9 + 3x9	7/63
	Protocol 18	6x23	6/138
	Protocol 19	4x(21) + 4x(4x17)	20/356
	Protocol 23	4x21	4/84
	Protocol 27	6x(5x9)	30/270
Anal	Protocol 01	1x5 + 1x4	2/9
	Protocol 02	1x31 + 1x29	2/60
	Protocol 32	1x5 + 1x5	2/10
Kaposi's Sarcoma	Protocol 09	7x6	7/42
Esophagus	Protocol 13	1x13 + 3x27 + 1x13 + 3x27	8/178

Table 4, shows for every cancer type, the maximum amount of days that a patient's beginning of a treatment could be delayed. The priority of each cancer type is stipulated by medical criteria, and considers three factors: if the patient is GES (Health Explicit Guarantees, priority established by the Health Ministry) or not, urgency level of the patient (where 2 is very urgent and 0 not very urgent), and improvement possibilities (where 2 is a high probability of improvement and 0 low or null). The priority score for every cancer type is calculated by adding these four parameters. It is important to mention that both the scoring scales and the method to calculate the priority were established along with the Chemotherapy team since, currently, there is no formal method to calculate this prioritization.

Table 4: Patient prioritization according to cancer type

Cancer Type	*Maximum Delay [days]*	*Priority*	*Justification*			
			GES	*Urgency*	*Recovery posibilities*	*Total*
Testicle	7	1	1	2	2	5
Colon	7	2	1	1	1	3
Colorectal	7	3	1	1	1	3
Rectal	7	4	1	1	1	3
Gastric	28	5	0	1	1	2
Kaposi’s Sarcoma Anal	14	6	1	0	0	1
Esophagus	14	7	0	0	0	0

Regarding the daily scheduling of patients, today the Chemotherapy Unit has two time blocks of patient care for treatment sessions. The first one, from 8 AM to 12 PM, and the second one, from 2 PM to 5 PM. For every day there is a list of patients that must be treated, and the head nurse determines in which chair and time slot each patient will begin its treatment, depending on the available space. If a patient’s treatment is extended beyond the length of the first time block, a corresponding chair is blocked for the rest of the day, and no other patient can use it afterwards.

1.11 Results

The scheduling of patients in time, which corresponds to the first part of the addressed problem, was programmed in Microsoft Visual Studio 14.0.23107.156, both for the current hospital method and for the methodology adapted from Sauré et al. (2012). The pattern generation for the patient scheduling was also done in Microsoft Visual Studio 14.0.23107.156, while the subsequent mathematical model was programmed in GAMS 23.5, using CPLEX as a solver.

1.11.1 Input Information

Based on the information contained in Table 3, some protocols were grouped by similarity, such as the case of protocols 35 and 36 for testicular cancer, or protocols 37 and 38 for colorectal cancer. Afterwards, the more frequent treatments in the patients' records given by the hospital, for each type of cancer, were selected, and around 11 groups or types of patients were finally determined (see Table 5). It is noteworthy that there may be more than one group for one type of cancer, such as the case of groups 3, 4, and 5 that indicate colorectal cancer for a patient, but differ in their treatment structure. On the other hand, for the case of gastric cancer, the opposite situation occurs, since there are just five protocols but only one group associated with this cancer. This is because all the patients presented the structure described by protocol 23, in the patient care record.

From the data showed in Table 5, we generated the arrival of patients per cancer type following a Poisson distribution (see Sauré et al. 2012). Afterwards, both scheduling methodologies were programmed, using the same generated patients database. In order to compare the performance of both of them, we performed a simulation that considered a booking horizon of 300 days and a planning horizon of 1000 days. Also, a period of warm up of 300 days was considered to evaluate the methodology in a state of regime (non-empty calendar). We ran 100 replicas and for each one of them the performance indicators defined were measured: delayed patients percentage (DPP), extra consultation slots used (ECS), and extra treatment slots used (ETS).

Table 5: Treatment groups used to evaluate the proposed methodology

Type	*Capacity requirements*	*Sessions/slots*	*Arrival rate [reqs./day]*	*Cancer*
1	3x(5x22)	15/330	0,071	Testicle (GES)
2	6x(5x11)	30/330	0,425	Colon (GES)
3	4x25	4/100	0,034	Colorectal (GES)
4	8x12	8/96	0,068	Colorectal (GES)
5	12x15	12/180	0,034	Colorectal (GES)
6	1x1	1/1	0,080	Rectal (GES)
7	4x21	4/84	0,009	Gastric
8	1x5 + 1x5	2/10	0,002	Anal
9	1x31 + 1x29	2/60	0,003	Anal
10	7x6	7/42	0,024	Kaposi's Sarcoma
11	1x13 + 3x27 + 1x13 + 3x27	8/178	0,009	Esophageal

1.11.2 Dynamic Programming Policy Results

Table 6 shows the results obtained after the simulation. For the metric DPP, it can be seen that in the hospital's case, from the 100 replicas made, in 43 of them between a 10% and a 20% of the patients were delayed, on average; while the posed methodology delayed more frequently, between a 40% and a 50% of the patients on average (63% of the replicas). Regarding metric ECS, in 46% of the replicas the amount of extra slots of medical consultation used, on average, was between 0.6 and 0.7 daily slots (that is, between 9 and 11 minutes); while with the posed methodology, in 48% this value was maintained between 0.5 and 0.6 slots (between 7, 5, and 9 minutes). Finally, for metric ETS is can be observed that for the case of the hospital 39% of the replicas required from 5 to 10 extra treatment slots (1.25 to 3 hours), daily, on average; while with the posed methodology this proportion was greater (53% of the replicas).

Table 6: Simulation results

	Frecuency			*Frecuency*			*Frecuency*	
DPP	*Hospital*	*Methodology*	*ECS*	*Hospital*	*Methodology*	*ETS*	*Hospital*	*Methodology*
< 10%	**34**	0	<0,1	0	0	<5	1	7
10%- 20%	**43**	0	0,1 - 0,2	0	0	5 - 10	39	**53**
20% - 30%	16	1	0,2 - 0,3	0	0	10 - 15	**34**	26
30% – 40%	6	**27**	0,3 - 0,4	0	2	15 - 20	24	12
40% - 50%	0	**63**	0,4 - 0,5	5	**20**	20 - 25	1	2
50% – 60%	1	9	0,5 - 0,6	**29**	**48**	25 - 30	1	0
60% - 70%	0	0	0,6 - 0,7	**46**	**25**	30 <	0	0
70% – 80%	0	0	0,7 - 0,8	19	5			
80% - 90%	0	0	0,8 - 0,9	1	0			
90% <	0	0	0,9 <	0	0			

Regarding the number of patients whose treatments' start were delayed, the hospital's method presents a smaller average percentage than the one obtained with the suggested methodology. This is due to the short-sighted approach used in Chemotherapy in order to schedule the patients, in which they are scheduled as soon as they arrive, and therefore, there are only a few cases in which patients are delayed. The suggested methodology, instead, aims to book care modules in the future. Thus, around a 45% of the patients are delayed to the maximum waiting time allowed.

It is important to note that the fact that the suggested method presents a higher DPP does not imply that its performance is low, since there is no explicit penalty for delaying the beginning of a patient's treatment within the allowed range. The method posed by Sauré et al. (2012) does consider a penalty for delayed days, which is implicit in the policy proposed.

The method suggested presents a saving in the amount of extra hours used in comparison with the method currently used by Chemotherapy. For the case of extra medical consultations slots (ECS) the amount of extra care slots is less than 1 on average, for every replica. It follows that, currently, the care capacity on behalf of the oncologist is appropriate.

On the other hand, the number of extra slots intended for chemotherapy treatments (ETS) are not enough to fulfill the current demand. For this simulation, the hospital's method has an average daily deficiency of 14±5 treatment slots (or 3.4±1.2 treatment hours), while the proposed method presents a deficiency of 11±4 treatment slots (or 2.8±1.2 hours). It is noteworthy that this results does not imply that the workday needs an extension of 3 hours, but rather that around 3 extra care hours are required, which could be effectuated in a parallel manner. Finally, the amount of extra consultation slots for a year was 378±47 (or 94±12 hours) and 333± 50 (or 83±12 hours) on average, for the hospital and the posed method, respectively; whereas the amount of extra treatment slots for a year was of 8,194±3,045 (or 2,048±761 hours) and 6,789± 2,939 (or 1,697±735 hours), on average. Using the proposed method, instead of the current methodology used in Chemotherapy, would allow saving a 20% of costs per extra hour.

1.11.3 Optimization Model Results

In order to implement the second part of the methodology, which corresponds to the daily patient scheduling, a calendar was made for one year, using the proposed method. To determine the performance of the mathematical model suggested, we solved the problem for a week that presents a profile which repeats in time (see Figure 6).

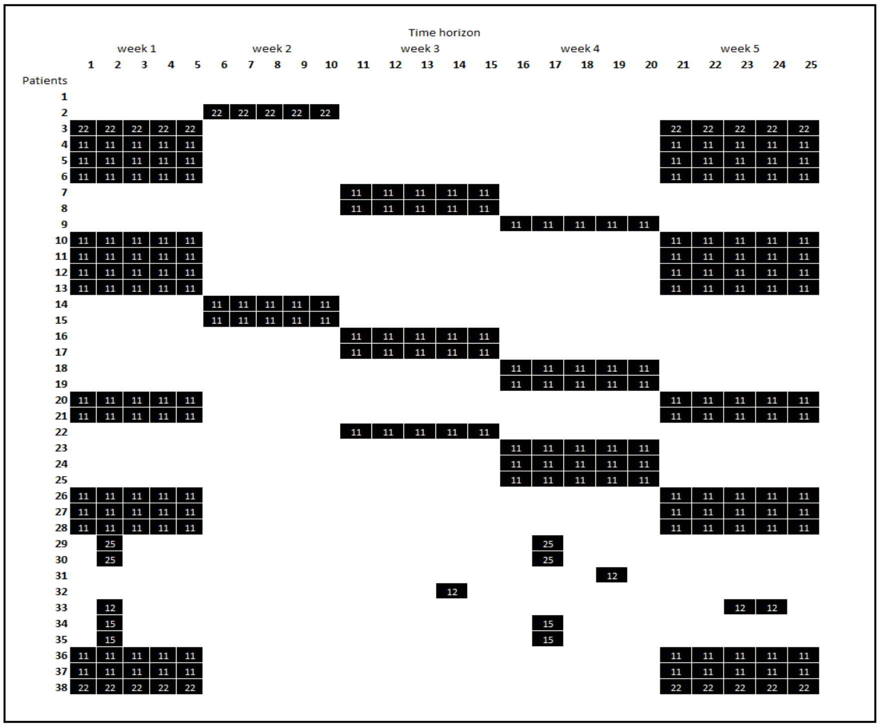

Figure 6: Extract of the generated calendar from the Sauré et al. (2012) method

For the chosen week, 83,195 patterns were generated in total, in a time inferior to 2 minutes. These patterns were cleaned, in order to remove those options that are not frequently used in practice. For example, an allocation for a chair with just one patient who starts its treatment session at the end of the day, or cases with more than three patients per chair[1]. After removing these type of cases, the number of patterns in total for the week is

1 Given the treatment structures and average session duration (11 slots), in most cases it is not possible to schedule more than 3 patients in the same treatment chair.

10,834. With this amount of patterns, it is possible to obtain an optimal solution for the problem, in just a few seconds; while with a traditional model (that is, without using patterns), it was not possible to obtain a solution, due to the lack of computational memory. The computer used to generate the patterns and solving the model was a 2.2 gigahertz Quad Core PC (processor Intel ® Core ™ i7-5200U) with 8 gigabytes of RAM.

Figure 7 a) shows the optimal solution obtained with the mathematical model and Figure 7 b) shows the solution that would be obtained with the method used by the Chemotherapy Unit today, both for the day with greatest demand in the week. The method currently used by the hospital consists of two time blocks in which the patients' sessions are allocated. If a session lasts longer than block 1's duration (in this case, patients P3 and P8), the chair will be blocked for the rest of the day, impeding other patients to receive their treatments in the same chair.

Table 7 contains the solution for two scenarios using the hospital and the proposed methods. The results obtained in both scenarios, where Scenario 1 presents a normal demand of patients and Scenario 2 a critical situation with a high demand of patients[2], show that the policy of fixed time blocks established by the hospital constrains the solution, which results in a significant loss of care capacity. The number of slots not used for patient care in the hospital Scenario 1 was 21% greater than the results obtained using our methodology, which implies that the proposed method manages a more efficient use of

2 To define a critical day, 21 colon cancer patients (each one of them requiring 11 care modules) were estimated as a maximum. Assuming a maximum of 3 patients per treatment chair, and a total of 7 chairs, this configuration is tight enough to need extra hours. For the generated calendar, this demand profile is found among the 10 profiles that are frequently obtained.

care capacity than the current hospital method. Thus, due to a better capacity management the proposed model achieves to serve the last patient 10 slots (2.5 hr) earlier than the hospital method and incurs in 83.3% less extra care hours.

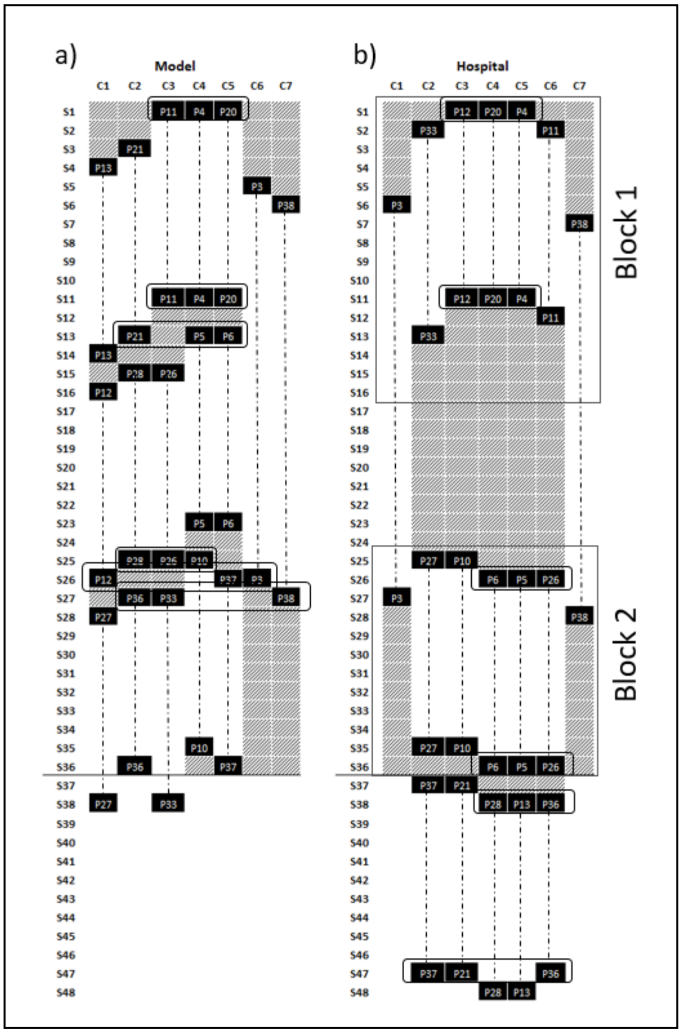

Figure 7: Results of the allocation of patients to treatment chairs, for a Thursday of a standard week.
The hatched area represents the treatment slots not used. The working day ends in slot 36, all the subsequent slots correspond to extra hours.

Regarding the use of lab hours, in Scenario 1 the hospital's method achieves a 22% less capacity usage in the day than our method and incurs in more extra lab hours the previous day, because in the hospital scenario patients with preparation constraints are scheduled early in the morning, therefore, their medication must be prepared the previous day. The extra hours needed should be externalized with an additional cost associated, which was not considered within the objective function of the model, since we assumed that it is not possible for the hospital to increase the lab's capacity.

Table 7: Optimization results for daily patient scheduling

		Chemotherapy Unit				Laboratory	
		FTLP [slot]	*EST [slots]*	*Number of patients using extra slots*	*Care Capacity Loss*	*Same Day Lab Capacity Usage*	*Previous Day Exceeding Slots*
Scenario 1:	Hospital Method	48	12	5	40%	64%	14
Normal day	Proposed Method	38	2	2	19%	86%	11
Scenario 2:	Hospital Method	49	68	8	32%	75%	60
Congested day	Proposed Method	46	18	4	12%	100%	58

It is important to mention that the capacity use depends strongly on the number of patients whose medication must be prepared the same day. That is to say, if a large number of patients of this type arrive, the difference between the optimal solution and the one provided by the hospital's method would not be significant, since the solution tends to be just one: use the same day all the available lab slots for patients whose medication must be prepared that day, and use the available hours of the previous day to prepare the medication of the rest of the patients.

1.11.4 Sensitivity Analysis

An important analysis based on these results is how different trade-offs perform considering different resources. In the example shown in Figure 7, the solution obtained by our model provides a low use of extra hours (4 care slots) given the demand of patients. However, in days in which this demand is greater, it is interesting to study the possibility of requiring extra resources, whether treatment chairs or nurses.

From the calendar generated through simulation, a categorization of the daily capacity use was made (in amount of care slots required), and based on this, we identified 24 demand configurations which will inevitably result in the use of a significant amount of extra hours (critical days) and which represent the 11% of all the scheduled days. From the critical days generated, the scheduling was made for a day in which 21 patients arrive, who require 11 care slots, and two cases were evaluated: i) allow the use of extra hours, and ii) do not allow the use of extra hours, but consider the option of adding extra treatment chairs, if necessary.

We used the configuration of Scenario 2 (see Table 7) to evaluate each case. The optimal solution found for the first case considers a workday that finishes 2.5 hours after the regular working hours, and also, that incurs in the use of 16 extra care slots. On the other hand, the results for the second case provide an optimal scheduling that requires increasing in 2 the provision of treatment chairs in order to reach a feasible solution, and thus, achieve to treat all the patients. In case ii) the 2 extra treatment chairs added enable to treat 4 patients, who in case i) are treated in a workday 2.5 hours longer, in which two more nurses are required to work in parallel. The trade-off between the acquisition of 2 extra treatment chairs and hiring 5 extra care hours of clinical nurses encourages the option of allowing overtime in the workday. It is important to highlight that this analysis also depends in the proportion of the critical cases that may occur. As it was mentioned before, the current demand of patients generated contains an 11% of critical cases. However, if the demand increases in the future and the resources available today remain constant, there will be a moment when the cost of hiring overtime for every critical day that occurs will be inferior to acquiring extra treatment chairs.

Finally, we analyzed the impact of adding one more nurse for case i), in which the use of extra hours is allowed. With this measure, it was possible to reduce in two slots the extra care capacity needed. Nonetheless, the additional extension of the workday did not suffer any changes, since it was not possible to relocate the entire session of a patient within the working hours. The addition of one more nurse does not have a significant impact in the reduction of the overtime cost, since a sufficient saving of care slots for a whole treatment session (which usually lasts several hours) is not achieved.

1.12 Conclusions and Future Work

This paper describes a methodology to address the scheduling problem of chemotherapy patients, which is divided in two stages: the first one consists in scheduling the medical appointments and treatment sessions of every patient throughout a time horizon; while the second one, addresses the daily scheduling of patients. In order to address the patient scheduling throughout a time horizon, we adapted the policy established by Sauré et al. (2012) for radiotherapy treatments, which indicates the prioritization levels of the patients and how these should be scheduled according to features of their treatments. Regarding the second problem of patient scheduling, a two-part approach was proposed, which considers the generation of treatment patterns and also, a mathematical model for pattern allocation that incorporates restrictions of nurse care capacity and care hours available in the lab. The methods can be applied in practice with the objective of reducing the functioning costs incurred by the Chemotherapy Unit, ensuring the compliance of medical standards of patient care.

The results of this work show that for the first stage of the problem the scheduling policy implemented overcomes the current method used by the hospital to schedule patients. Regarding the costs' impact, the method proposed in this paper manages to reduce in a 20% the operational costs of the hospital, due to less extra treatment hours needed.

On the other hand, the proposed daily scheduling method for patients presents an improvement of 21% in care slots usage and 22% in lab slots usage for an average demand day with respect to the current methods applied to the use of resources. This translates in a reduction of both extra hours used and workday duration. The solutions of both stages of the posed methodology were obtained at a resolution time of seconds (or minutes for certain cases of pattern generation), which implies that the developed method is applicable in practice, and it would allow real improvements in the Chemotherapy Unit functioning.

This work does not explicitly include waiting costs of patients due to the delay in their treatments' starts, since the policy of Sauré et al. (2012) already includes this cost in the problem modeling. Therefore, when implementing the policy, the cost of delaying a patient is implicitly considered. Regarding the daily scheduling of patients, an aspect to emphasize is that since the data of all patients was no available, it is not possible to conclude whether an additional nurse is needed. Although there was no major impact observable when increasing to 1 de current staff of nurses, the effect may be different if the demand is greater, since the restriction of not treating a certain number of patients in a parallel manner would be an active restriction, turning into a bottleneck. The last issue to consider is related to the case in which it is possible to allocate more than 3 patients in a treatment chair, since the amount of generated patterns increases exponentially and complicates the computational implementation. Therefore, for these cases, it will be necessary to consider more efficient methods for scheduling, or pattern generation.

Further work extensions consider alternative schedules for laboratory dedication to the preparation of medication, in order to measure the impact of the daily patient scheduling, including the randomness of medication preparation times and the daily no-show factor. Also, it could be considered in further work to incorporate the clinical nurses intervention in several opportunities during a session, and not only at the beginning and end of it. Finally, there may be incorporated mixed treatments in the future, in which a combination of chemotherapy and radiotherapy are required, which implies the consideration of a new significant restriction of resource compatibility.

2. APPOINTMENT SCHEDULING AND PATIENT PROGRAMMING IN CHEMOTHERAPY: A CASE STUDY IN A CHILEAN HOSPITAL

2.1. Motivation

Within the fields that Operation Research addresses, there is an area focused on the resolution of problems related to scheduling. This consists in allocating resources in a certain time interval, which is subject to specific conditions, in order to satisfy in the best possible way a certain objective (Wren, 1996). The scheduling problems are frequently present in the area of health, where they have been approached from different perspectives: to schedule medical staff shifts (Burke et al., 2004); to allocate hours for the use of scarce resources, such as operating rooms or laboratories; and to schedule appointments of health care to patients (Cayirli and Veral, 2003). Within this last category, there is a specific problem of scheduling appointments for medical treatments, such as dialysis, chemotherapy, or physiotherapy.

The problem that this investigation addresses is the one faced today by the Unit of Chemotherapy of the Salvador Hospital, in Santiago of Chile. According to the American National Cancer Institute, chemotherapy is a type of cancer treatment that uses pharmaceuticals in order to destroy cancer cells. This treatment can be prescribed to a patient for two reasons: to cure cancer (healing), or to relieve the disease symptoms (palliative). This type of treatment consists of several sessions of varying duration, which can be accompanied by other treatments, such as radiotherapy or surgery.

There is a medical team that determines the treatment for each patient, based on the type of cancer the patient presents and the severity in which it is found. If a patient has possibilities for improvement, a healing treatment will be prescribed, which includes chemotherapy, radiotherapy, surgery, or a combination of these. On the other hand, if a patient does not have any chance of recovery, a palliative treatment will be prescribed, in which pharmaceuticals will be provided in order to relieve the patient's symptoms. Also, a patient who has not evolved successfully during its healing treatment falls in this category.

The scheduling of chemotherapy patients may consider two dimensions: the scheduling of sessions in an infinite horizon of time, and the daily scheduling of patient care. Each of these dimensions presents several challenges from the operational viewpoint.

Concerning the first dimension, it is required that the sessions follow the predetermined structure, for the treatment to be effective. Hence, once the appointment is scheduled, it is not possible to change it in case there is no medical capacity to treat the patient. This implies that it is possible that there is no allocation of patients, whose treatments fit perfectly and no modules are lost (Sauré et al., 2012). Furthermore, there are some types of cancer with a higher priority care than others, whether for urgency, speed of disease development, or for improvement possibility. Therefore, it is not possible to schedule patients under a First In First Served policy.

The second dimension, which is related to daily chemotherapy patients' care, presents two great challenges. Firstly, each chemotherapy treatment uses a determined quantity of limited resources: hours spend in a treatment chair, considering both oncologists and nurses. In this vein, an important aspect to consider is the impact of the laboratories operations in the daily management of chemotherapy patients. In the case of the Salvador Hospital, the Unit of Chemotherapy works directly with Central Mixing, the laboratory in charge of preparing the necessary pharmaceuticals to treat the patients. This laboratory has limited time capacity, aimed to prepare the hospital's orders, which constrains how patients should be managed on a daily basis. On the other hand, chemotherapy treatments state that certain pharmaceuticals can be prepared beforehand (usually the day before treating a patient), and others must be prepared the very same day in the morning. Therefore, there is a limitation that requires treating certain patients from a specific time onwards, which increases the complexity of the problem.

The second challenge is the complexity of the problem structure itself. The daily scheduling of patients is categorized as a problem of parallel machine programming, where each treatment chair corresponds to a machine, and the patients' sessions to tasks that must be assigned to each chair. This problem is NP-complete (Du and Leung, 1990), and must be solved for numerous parallel machines, which implies an extensive associated combinatorial, and therefore, requires a different approach from the classical mathematical modelling.

Nowadays, the methodology used by the Unit of Chemotherapy, in order to schedule the patients and schedule daily treatment sessions, consists in the use of extra hours of care, and postponing the initiation of certain patients' treatment. This is due not only to the lack of care capacity (both in medical hours and treatment modules), but also it is the outcome of an unplanned management of care hours, nurses shifts and treatment chair hours. The costs of not having a proper scheduling of patients is monetary, as it implies and extra expense for the hospital to supplement the lack of capacity with extra hours; as well as social, as certain patients have to delay their treatment initiation due to the lack of capacity, which decreases their chances of recovery (Ragaz et al. 2004).

There are publications available in literature, which state that a delay in the treatment initiation of a patient has detrimental effects in their chances of survival, either because there is a progress in the development of the tumours, or because the symptoms worsen rapidly over time. This happens, for example, in patients with testicular or colon cancer, where both diseases are quite frequent, and develop rapidly over time (O'Rourke and Edwards, 2000; Chen et al., 2008; Sauré et al., 2012; Song et al., 2013; McLaughlin et al., 2012; Bos et al., 2015; Bernard and Sweeney, 2015). Therefore, relying on a formal, efficient, and robust methodology that allows the scheduling of patients and plan the daily health care is essential in order to decrease the extra expense of the Unit of Chemotherapy.

2.2. Literature Review

The Operations Research field has approached the different problems that arise in health management in multiple researches. Some of these problems correspond to doctor or nurse rostering, managing waiting lists, and the scheduling of medical consultations and treatments. Timetabling of patients for medical appointments or for treatments is a problem that is frequently present in healthcare, where the objective is to find a configuration for appointments that optimizes certain indicator (number of patients treated, use of overbooking, clashes in the timetable, etc.) under a scenario that presents restricted resources and uncertainty. The problem is present in diverse medical fields, such as the scheduling of patients for haemodialysis, radiology, surgery, or chemotherapy (Cayirli and Veral, 2003).

This research focuses on the scheduling of chemotherapy treatments and addresses two main issues: the scheduling of patients through time and the daily scheduling of these patients' care services. The first issue refers to the allocation of medical hours or treatment sessions in a time horizon. Within the available techniques to solve scheduling problems, dynamic scheduling considers variables that are subject to random events and it has been used to address problems not only in healthcare. For example, it has been used in the industrial sector to solve staff planning problems, specifically the scheduling of working shifts that consider days off, part-time workers, absenteeism, among others (Ernst et al. 2004); and in the airline industry to determine commercial flights itineraries (dates, boarding gates, and port of landing) (Warburg et al. 2008, Jiang and Barnhart, 2009).

In healthcare, this method has been used to coordinate the daily allocation of medical resources (medical and nursing care) to patients in a clinic (Gupta and Denton, 2008), to schedule medical care and treatments for patients with different care priorities (Patrick et al., 2008, Sauré et al., 2012) and to schedule patients considering no-show (Liu et al., 2010).

The second issue that this research approaches refers to the scheduling of the daily functioning of the chemotherapy unit. This problem can be formulated as a machine programming model which can be divided into different categories: machines in series or in parallel, independent or dependent on each other, uniform or different processing times on each machine, among others (Graham et al., 1979). The daily problem that the hospital has to solve corresponds to a machine programming problem with parallel machines, dependent on each other, where the objective is to minimize the moment in which the last patient ends its treatment.

Among the existing works we can mention Yalaoui and Chu (2001), who solved the machine-programming problem in parallel through a Branch and Bound algorithm, Anghinolfi and Paolucci (2006) who present a hybrid metaheuristic which combines Tabu Search and Simulated Annealing in order to achieve an approximation to the solution of the problem, and Li et al. (2011), who suggest different theoretical approaches to the solution and a heuristic of resolution based on Simulated Annealing. Other authors that suggest the implementation of heuristics in order to solve the machine-programming problem are Bilge et al. (2002), who present a heuristic based on Tabu Search.

Between the publications available in literature, it was not possible to find any in which the programming of machines model was used in order to solve the scheduling of patients problem. However, there are publications that try to solve this problem (or variations of it) through other approaches. Among the works that are closer to solve the problem that this research addresses we could mention Conforti et al. (2008) and Condotta et al. (2014). The first ones present the daily scheduling problem of radiotherapy patients, and propose an optimization model that maximizes the number of treated patients. The second authors mentioned solve both the scheduling of patients through time problem and the daily scheduling of patients' care services.

The scheduling problem of treatments has been approached in literature considering diverse features, such as session length, if multiple types of priority or capacity requirements for patients are included or if the use of overtime is allowed or the horizon of scheduling is finite or infinite (Patrick et al., 2008; Conforti et al., 2008; Conforti et al., 2010; Sauré et al., 2012.; Condotta and Shakhlevich, 2014). Concerning the configuration for medical treatments, Cayirli and Veral (2003) perform a categorization of the types of treatments in healthcare (individual block of fixed length, variable length, multiple blocks, etc.).

There are different types of treatments, besides chemotherapy, such as dialysis, physiotherapy, and radiotherapy. These treatments differ from chemotherapy, since they have different structures and requirements. In the case of dialysis, for example, the attendance of the patient to the treatment centre is regular, since the patient needs the treatment in order to survive daily; physiotherapy on the other hand, is similar to chemotherapy since both treatments vary depending on the patient's diagnosis but differ from each other in that physiotherapy treatments allow adding sessions and changing the time separation between these (Ogulata et al., 2008; Griffiths et al., 2012). Finally, radiotherapy treatments can be mentioned, which constitute a particular case of chemotherapy in that they use not only medication, but radiation as well. Also, the sessions' features conform to the patient's condition (tumours locations, patient's dimensions, and health conditions) (Conforti et al., 2008).

Literature referring to the scheduling of cancer treatments (both chemotherapy and radiotherapy) is divided into two currents of thought: one that approaches the problem in a static manner and another one that solves the problem in a dynamic manner. In the static problem, the scheduling choices are made at the beginning of the evaluation period. On the other hand, the dynamic refers to the methods used for scheduling appointments for patients before they set a day for their treatments, when the demand is yet uncertain.

Among the publications that address the scheduling problem in a static manner, the work of Conforti et al. (2008) can be found, who propose a mathematical model to solve a radiotherapy session scheduling problem. The authors consider a base case in which the calendar does not contain previously scheduled patients. Later, they pose an extension in which it is consider the case where the system does not start empty and allows rescheduling patients that were previously scheduled. The authors also made an extension of this publication, in which they consider priorities for patients and a block of flexible duration length (Conforti et al., 2010).

Petrovic and Leite-Rocha (2008) address the radiotherapy-scheduling problem as well, and they consider two rules for scheduling: forward and backward. The former refers to begin scheduling patients from their waiting deadlines, while the latter refers to scheduling patients as they enter the system. This research aims to establish rules or policies that enable scheduling in an easy and rapid manner, without impairing the quality of the solution. Among recent publications that aim for this type of perspective, Patrick et al. (2008) and Sauré et al. (2012) can me mentioned, who pose scheduling policies under a dynamic approach. Both publications consider an infinite horizon of time, multiple priorities, and the use of overtime.

The scheduling of chemotherapy treatments may address not only the scheduling of sessions, but also the manner in which these patients must be treated daily. A work already available in literature, which considers both stages, is the Condotta and Shakhlevick's (2014) one. They not only schedule patients in a finite horizon of time, but they also determine the sequence of activities for the personnel during the day. However, unlike our research, the authors consider a static approach for scheduling the patients' sessions, and they do not include in the daily timetabling the use of laboratory capacity for the medication preparation.

In the same vein of daily patient scheduling, the work of Le et al. (2015) can be mentioned, who solve the scheduling problem of hematology and chemotherapy treatments. For this, the authors propose a mathematical model first and a Tabu Search heuristic in a second stage. The problem solved by the authors considers a static scheduling, in which the treatment sessions of the patients are allocated together, disregarding the uncertain future demand. On the other hand, the problem solved by Let et al. (2015) aims to optimize the allocation of the nurses' workload, and disregards the required time for the medication preparation for the patients, two issues that differ from the approach proposed in this research.

2.3. Problem Definition

2.3.1. Characterization of Chemotherapy Treatments

A chemotherapy treatment is composed by a determined amount of sessions, in which the patient is provided with a specific combination of medication. These sessions have a defined length, which may vary according to the treatment or even for a same treatment, and are held throughout a time horizon according to a cycle that could be every month or every two weeks, for example. The established structure for the treatment should be respected in order for the treatment to be effective, therefore, it is not possible to reschedule sessions if there is no capacity for a certain day.

Figure 1 provides two examples, where each number within the table indicates the amount of time slots needed for a session in the appointed day. We determined based on the diverse existing treatments that the minimum duration unit for a treatment is 15 minutes, so each time slot corresponds to a 15 minutes block. The first case (colorectal cancer) has a cycle every two weeks, in which the patient is provided a session of 3 hours and 45 minutes that should be repeated twelve times in order to complete the treatment. In the second case (esophageal cancer) the treatment is monthly, and the patient must be provided 4 consecutive sessions of varying length, scheme that should be repeated twice.

Colorectal cancer: 12 cycles, cycle: 15 days

	mon	*tue*	*wed*	*thu*	*fri*
week 1	**15**	0	0	0	0
week 2	0	0	0	0	0
week 3	**15**	0	0	0	0
week 4	0	0	0	0	0

Esophageal cancer: 2 cycles, cycle: monthly

	mon	*tue*	*wed*	*thu*	*fri*
week 1	**13**	**27**	**27**	**27**	0
week 2	0	0	0	0	0
week 3	0	0	0	0	0
week 4	0	0	0	0	0

Figure 1: Graphic representation of the cycle structure of two different chemotherapy treatments

For each session (or set of sessions corresponding to one week) the patient must be treated firstly with the treating oncologist, who requests for an examination in order to validate that the patient is in condition to receive a treatment. Therefore, every time a cycle begins an hour for medical consultation is also needed, which fluctuates between 15 and 45 minutes. This consultation can only be held within the same week in which the patient will be treated, because if there were a longer time separation, the patient's examination would no longer be valid. Finally, each session needs a determined amount of lab slots in order to prepare the medication, which requires in certain cases to be prepared the very same day.

2.3.2. Available Resources

The Chemotherapy Unit is composed by one oncologist, three clinical nurses who are in charge of executing the treatments, and seven treatment chairs. The oncologist works twice a week, has a care capacity of 36 slots of 15 minutes each, and the average length of a consultation corresponds to two slots (30 minutes). On the other hand, each clinical nurse and treatment chair is available for 36 slots every day. The lab receives preparation orders for a certain day until the previous day at midday. It also dedicates a number of time slots in the morning to prepare the medication that requires to be made the very same day.

2.3.3. Patient Scheduling Throughout a Time Horizon

Patients arrive randomly to the Chemotherapy Unit, where they are evaluated by a group of oncologists who determine the type of chemotherapy treatment each patient has to undergo. Every patient has to go through a previous process in order to start its treatment, which may take one or several sessions with the treating oncologist. This research will not include this stage, and the entry day of a patient to the system will be considered as the day in which all the previous stages of treatment approval are already done.

Since the treatments have a fixed structure that indicates the amount of sessions and the gap between them, the decision is when does each patient start its treatment and it depends on the available capacity of i) time slots for patient care (medical attention) and ii) time slots for patient care in every treatment chair. Patient scheduling is done from one week to another, that is to say, every week patients are admitted and scheduled at the end of that same week for future days.

It is noteworthy that for every type of cancer there is a maximum time stipulated to postpone the start of a patient’s treatment, due to the rapid development of cancer. Furthermore, every type of cancer has a priority level assigned under medical criteria, which considers factors such as the severity of the disease, improvement probabilities, and additional constraints established by the Ministry of Health. Therefore, the timetabling must respect this prioritization when allocating patients throughout the time horizon.

Example 1. Consider a small example of 10 patients arriving to the system throughout one month. In Figure 2 two timetables can be observed, where the upper one corresponds to the patient care scheduling (oncologist session), and the lower one to the treatment sessions. Each row corresponds to the timetable of one patient, and the hatched area indicates weekend days in which there is no patient care. The arrival day of each patient to the system is known (red blocks), and based on this information a medical appointment is scheduled with the treating oncologist, starting from the week after its entry (see upper timetable). There are cases in which the patient may be delayed beyond the week after its entry, such as the case of patients P2 and P8. Patient P2 enters during the first week, however, its first session is scheduled for the third week. Likewise, patient P8 enters the third week, but the start of its treatment is postponed at least two weeks. These delays are due to the non-existing capacity of patient care for a consultation to take place prior to the session the week after the patient’s entry. It can be observed that the lower timetable structure, corresponding to the treatment sessions, depends on the scheduling with the oncologist. As a general rule, the consultation with the treating oncologist must take place the same week of the treatment sessions. Nonetheless, there are some treatment schemes (as the colon cancer one) that require five consecutive sessions. Therefore, an exception has to be made for these cases, and the consultation takes place the previous week, as late as possible.

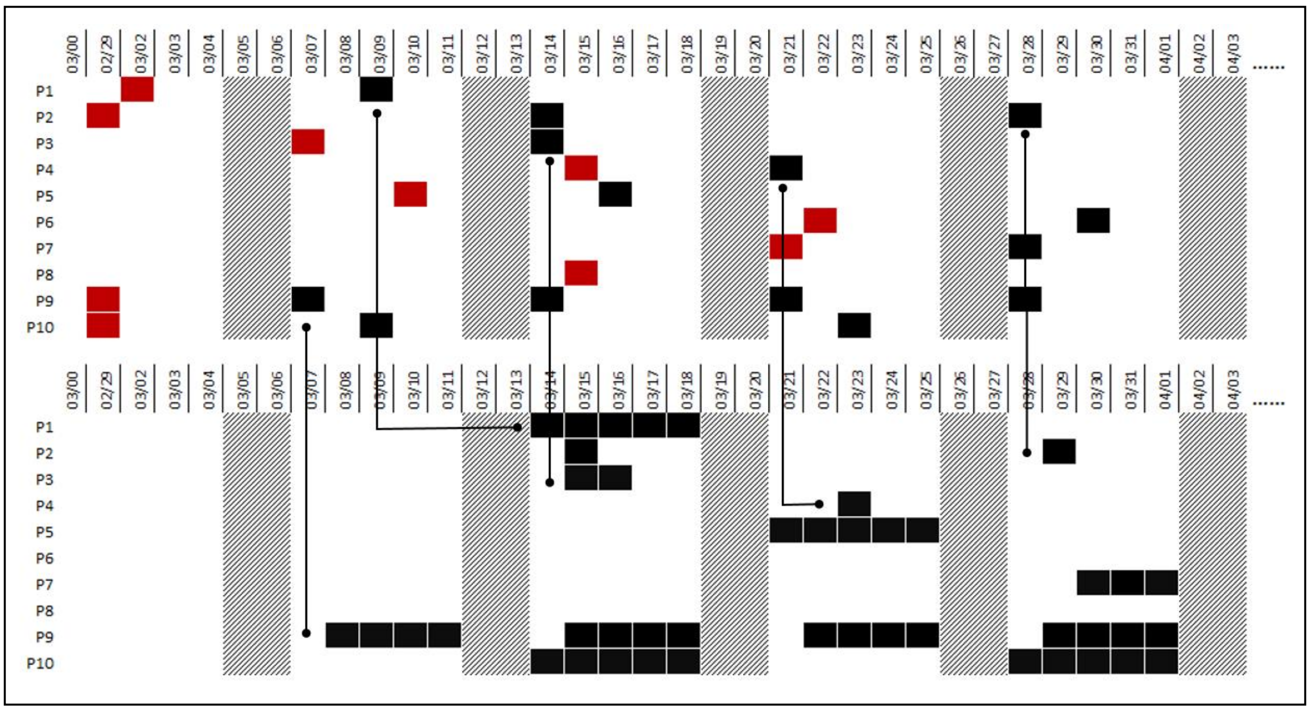

Figure 2: Example of the arrival and scheduling of medical appointments of patients for a month of the time horizon

In order to measure the impact of the scheduling decisions, three metric units were established: Delayed Patients Percentage (DPP), Extra Consultation Slots (ECS), and Extra Treatment Slots (ETS). The first two metrics are related to the service given to the patients with respect to the waiting in order to begin their treatment, and to the saturation level of the system, because the constant delaying of the patients indicates there is a lack of patient care capacity. The third metric allows the quantification of the missing capacity and identifying if the scarce resource is the amount of medical hours or treatment hours. The final result of this first stage is the allocation of patients to their first day of treatment, and therefore, since there is a specific protocol for every patient that defines the treatment structure, the complete agenda of the sessions for each patient is determined. It is possible to build the whole calendar with this information, and determine for each day which patients must be treated.

2.3.4. Daily Patient Scheduling

The procedure used by the hospital in order to achieve a daily planning begins with deciding which patients and when will they be treated in each of the treatment chairs. Once this allocation has been done, there is a list of chores per chair, determined by the treatments of the corresponding patients. This list of chores is assigned to the clinical nurses, which results in a sequence of daily chores for every nurse. It is noteworthy that, as a general rule, if a nurse starts treating a patient, it must perform all the stages of the treatment that correspond to that patient. However, in the case of the hospital where this research was conducted, it is allowed for a patient to be treated for more than one nurse. Therefore, it is necessary that at least one of the nurses is available in order to start a treatment, and that this or other nurse is available to finish it.

A further significant condition that is considered in this research is the laboratory service capacity. The preparation of medication is done by only one chemist in an external lab, who receives preparation orders in determined hours, and dedicates a limited time to prepare these orders. The lab can prepare the medication of one day the day before since midday henceforth, or the very same day in the morning. Also, certain slots of the previous day in the morning could be used, if they are available and there is lack of capacity. In case all the available capacity of the lab is used (capacity given by the chemist availability), the preparation of the medication will be externalized to another lab, which implies an additional cost for the hospital.

Example 2. Figure 3 shows a scheduling of patients for a random day in Chemotherapy. The patients that should be scheduled and number of slots required is known information, as well as those whose medication must be prepared for that same day. The preparation time for medication fluctuates between 30 minutes to 2 hours. Diagram a) shows a timetable for 13 patients, of whom only two (P3 and P10) require their medication prepared the same day. For this example, 3 clinical nurses were considered, and the slots in which the resource nurse is used at full capacity can be observed in the diagram. The hatched area corresponds to the patient care time that was not used. Given the characteristics of the treatments and the restriction of not exceeding a maximum of nurses, it is not possible to distribute the patients in a way that they fit perfectly and no slots are lost during the day. Diagram b) shows the lab hours used the day before (left scheduling) and for the same day (right scheduling) of these same patients. The example considers for day *n* a lab capacity of 2 hours (8 slots) in the morning of the *n* and *n-1* days, and 4 hours in the afternoon (16 slots) for day *n-1*. It is possible to see that all the lab slots of both mornings are completely used, and that day n-1 in the afternoon is collapsed, which implies externalizing the medication preparation to another lab for patients P12, P26 and

P11. Furthermore, it is possible to see, in case there is available capacity in the morning of day n, that it is not possible to reschedule any patient (in this case, P6 and P26 cannot be treated the day before, because there would not be time to prepare their medication), which reflects that deciding at which time to schedule each patient, regarding the lab restrictions, is not trivial.

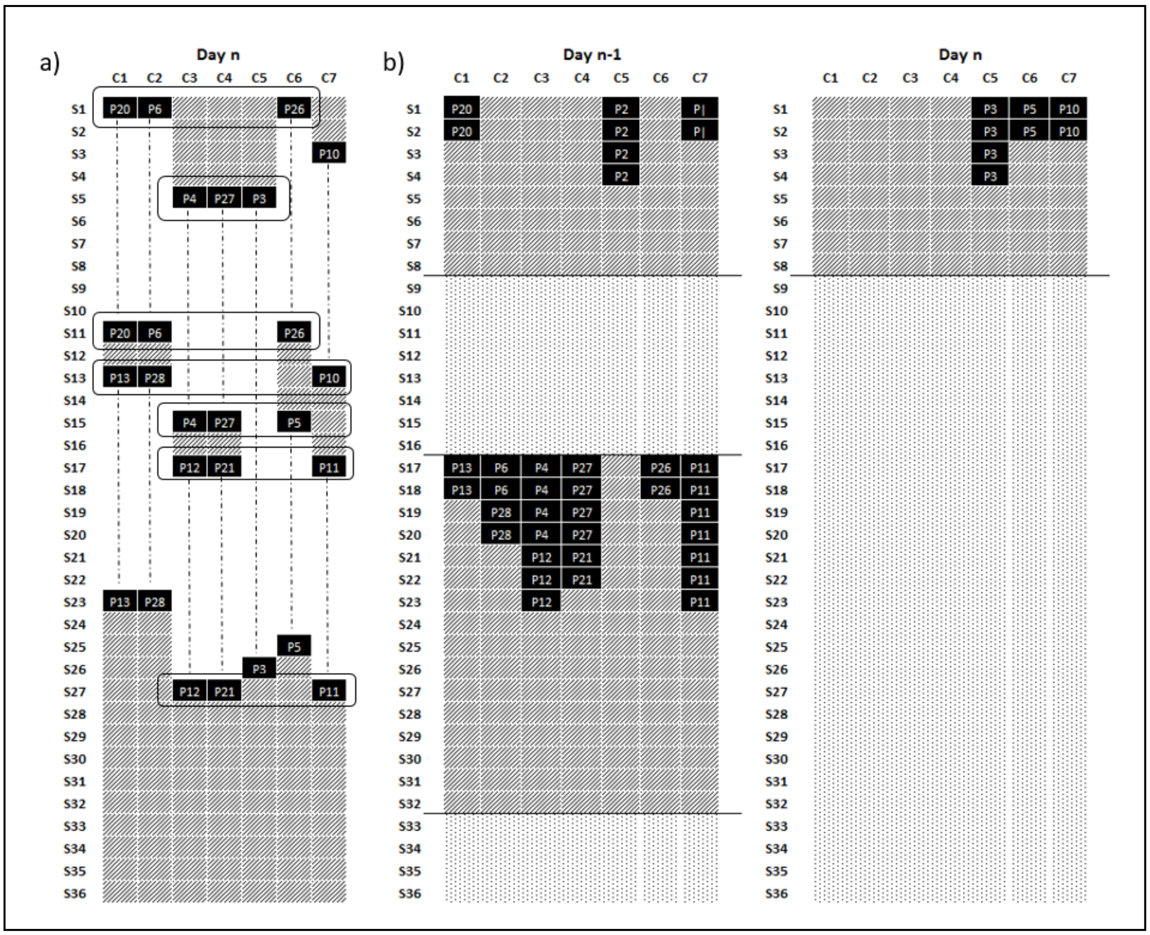

Figure 3: Example of patient scheduling for any day of 36 time slots (from 8 AM to 5 PM)

In order to measure the impact of the proposed method to schedule patients and compare it with the one used by the hospital nowadays, two metric unites were determined: finishing time of the last patient (FTLP), and extra slots used in order to treat the patients

(EST). The former is related to the number of extra hours incurred by the Chemotherapy Unit, while the latter indicates the amount of extra capacity (in care slots) needed so extra hours are not required. It is important to note that it is possible to increase the care capacity not only by increasing the amount of daily worked hours or treatment chairs, but also increasing the lab availability.

2.4. Solution Approach

2.4.1. Dynamic Patient Scheduling

In order to schedule the patients throughout a time horizon and determining the days in which they have to attend to a session, we implemented the model posed by Sauré et al. (2012). This method solves a scheduling problem of radiotherapy patients through the formulation of a Markovian Decision Process, which considers an infinite time horizon, multiple appointments, sessions of diverse lengths, and the use of overtime.

The methodology the authors propose aims to minimize three components: cost of starting a treatment a certain day, cost of overtime usage, and cost of delaying the scheduling of a certain type of treatment. The method allowed the identification of the following scheduling policies for radiotherapy treatments:

- Schedule the greatest amount of demand the first day available, and the rest starting since their deadlines for beginning their treatments.
- The greater the number of sessions, the treatment should be scheduled earlier.
- Those treatments with shorter sessions should be scheduled further in the future.

- The more urgent treatments, or with fewer time allowed to begin, should be scheduled as soon as possible.

Since radiotherapy and chemotherapy treatments consider in their structures the same conditions (in fact, radiotherapy treatments are a particular case of chemotherapy), the arrival of patients to the system in both cases behaves according to a Poisson distribution, and since Salvador Hospital considers the same costs to decide how to schedule the patients, it is possible to adapt the policy posed by Sauré et al. (2012) to chemotherapy treatments.

In order to implement the scheduling policy, it is necessary to define a category for the diverse treatments that the hospital currently has. This categorization is done based on the similarities of treatment structures, which include the amount of slots, cycle length, number of sessions and their durations. Once the treatments are grouped by type, two parameters must be established: booking horizon, which corresponds to the time horizon in which patients will be scheduled; and planning horizon, which corresponds to the whole time horizon in which patients will be scheduled. The planning horizon should consider at least the number of days as the booking horizon, plus the days of the longest treatment. That is to say, the most extreme case is considered, in which a patient with the more extensive treatment has its first sessions the last day of the booking horizon. Once the patients' categories and the time horizons are defined, the scheduling suggested by Sauré et al. (2012) is conducted as follows:

Step 1. Register the patients' arrival in one week. The patient scheduling will be conducted the last working day of a week.

Step 2. Order the patients in a queue considering the following elements, prioritizing according to the mentioned order: medical criteria (urgency and improvement possibility, established by the hospital), waiting time allowed (lesser time, greater priority), number of sessions (greater number of sessions, higher priority), and length of sessions (greater session length, higher priority). Thus, if there are two patients, one with a maximum waiting time of 14 days and 10 treatment sessions, and another one with a waiting time of 7 days and 8 sessions, the latter should be scheduled before, in spite of its less number of sessions, due to its shorter waiting time allowed.

Step 3. First, allocate the patient care hours starting from the first patient in queue. The first patient should be allocated in the first slot available, and so on, until there are no more available slots in the week.

Step 4. Allocate the rest of the patients starting from their deadlines.

Step 5. Considering the patient care allocation, distribute each patient's treatment hours. Each session can only be scheduled from the day after the consultation, and must be allocated within the same week of that consultation.

This scheduling policy differs from the one currently used by the hospital, since the latter conducts a short sighted allocation. That is to say, the medical appointments are scheduled according to patient arrival and no further capacity is booked in advance. However, it is important to highlight that in both cases there is a prioritization of patients, but in the hospital's case this is only based on medical criteria (urgency and improvement possibility). When implementing this scheduling policy, two calendars are obtained. One contains the days when each patient must attend to a medical appointment, and the other one indicates which days correspond to a session. This information is an input for the second stage of this methodology.

2.4.2. Pattern Generation for the Daily Scheduling of Patients

The daily scheduling of patients consists in determining a care order for a list of patients who have to be treated on the same day. This care order indicates in which treatment chair each patient has to receive its treatment and in which time slot. Therefore, for each chair a sequence of patients, who have to undergo chemotherapy sessions of varying length and different medical requirements, is determined. Treatment chairs work in parallel, so it is possible for several patients to be treated simultaneously, as far as there are available nurses. Finally, every treatment session specifies a time for the preparation of medication that could be produced the day before the patient's session or the same day in the morning. This time determines the possible time slots for a patient to start its treatment.

The decisions that have to be made present a challenge from the computational capacity viewpoint that is needed in order to solve the problem to optimality. In Example 2, which considers 7 treatment chairs, 14 patients during the day and 36 slots, the number of variables that indicate the allocation of patients, as well as the sequence in which they should be treated, is 9,359, and the number of corresponding restrictions is close to 78,403. An example of this dimension could be solved in a considerable time (more than one day) if there was a significant computational capacity, which is not applicable to the hospital's situation, as they have to solve this problem on a daily basis. Given the complexity of the problem structure, which presents a combinatorial that rapidly grows if more patients, chairs, or slots are considered, it is necessary to propose a new methodology to solve the problem.

We define treatment patterns in order to address the problem. A pattern corresponds to a possible allocation of patients to any chair, in which the sequence of patients and the slot in which they will start their treatments is indicated. To construct the patterns it is necessary to know what patients will be treated that day and how many slots their respective sessions require; information that is already known since it is the result of solving the previous scheduling problem. Then, it is possible to determine all the feasible combinations (or groups) of patients for one treatment chair, which works a certain amount of slots per day (see Table 1). Once the feasible combinations for patients who can be allocated to one treatment chair have been determined, treatment patterns are generated on this basis. For each combination of patients there are multiple possibilities to place them in sequence. Moreover, the problem allows for these patients not to be necessarily treated consecutively. That is to say, each patient may begin its treatment considering a wide range of scheduling options. In order to build a pattern, all the possible permutations of a specific combination of patients for one chair must be listed.

Table 1: Generation of some feasible combinations on the basis of 15 patients for one treatment chair that works for 36 slots (9 hours), daily

Pacient	*Session duration (15 min slots)*
P1	10
P2	10
P3	5
P4	11
P7	25
P9	10
P10	10
P11	10
P14	5
P15	11

Some feasible combinations:	*Patients*	*Total slots*
combination 1:	P1, P2, P3	25
combination 2:	P9, P10, P11, P14	35
combination 3:	P12	22
combination 4:	P5, P6	34
combination 5:	P13, P14	9
combination 6:	P3, P8, P13, P14	16
combination 7:	P7, P8	27
combination 8:	P9, P10, P11	30
combination 9:	P12, P4, P8	35
combination 10:	none	0

Example 3. Figure 4 shows 10 possible patterns for the combination P1, P2, P3. Every pattern indicates both the order in which the patients will be treated, and the slot in which each one begins its treatment. It is noteworthy that since each patient may start its treatment in different slots, the number of feasible permutations for each combination of patterns increases rapidly. For this example that considers only one combination (P1, P2 and P3), the amount of possible patterns is 20,956. If the example is considered for a day shown in Table 1, where there are 10 combinations, the amount of patterns for one day reaches 2,170,723. Therefore, for an example with a greater amount of combinations, the number of possible permutations easily reaches the million scale.

2.4.3. Optimization Model for the Daily Scheduling of Patients

The mathematical model that corresponds to the problem of determining the order in which each patient will be treated in every chair, and the slot in which they start their treatment, combines two decisions: allocation of patients to chairs, and sequencing of patients in a treatment chair. These two decisions together generate an unmanageable combinatorial from the computational viewpoint. Building patterns allows to diminish the number of problem variables, since the possible sequences of patients are given to the model as an input, and the only decision left is whether to allocate each pattern to each treatment chair, in order to comply with the corresponding restrictions.

This problem considers a set of patients J who should be treated on day t. Each day is divided into a number of 15 minutes slots contained in set M. For every day there is a set of patterns P, which contains all the feasible allocation patterns for day t. Finally, sets S and T correspond to the amount of treatment chairs at disposal and the number of periods (days) for which a scheduling is required. In order to obtain the solution for a specific day, it is necessary to consider at least two periods of time, because while the patient care is during day t, there are lab slots of day t-1 in which the medication for day t might be prepared.

To consider the resources of the Chemotherapy Unit, the following parameters are defined:

- NE corresponds to the number of nurses available for patient care.
- $\beta_{t,m}$ is the binary parameter that equals 1 if the laboratory is busy during period t and slot m, and 0 otherwise.
- QL_j indicates for every patient j how many lab slots are required to prepare the medication needed (information established in the corresponding treatment protocol).

- α_j binary pattern that equals 1 if the medication of patient j has to be prepared the same day, and 0 otherwise.

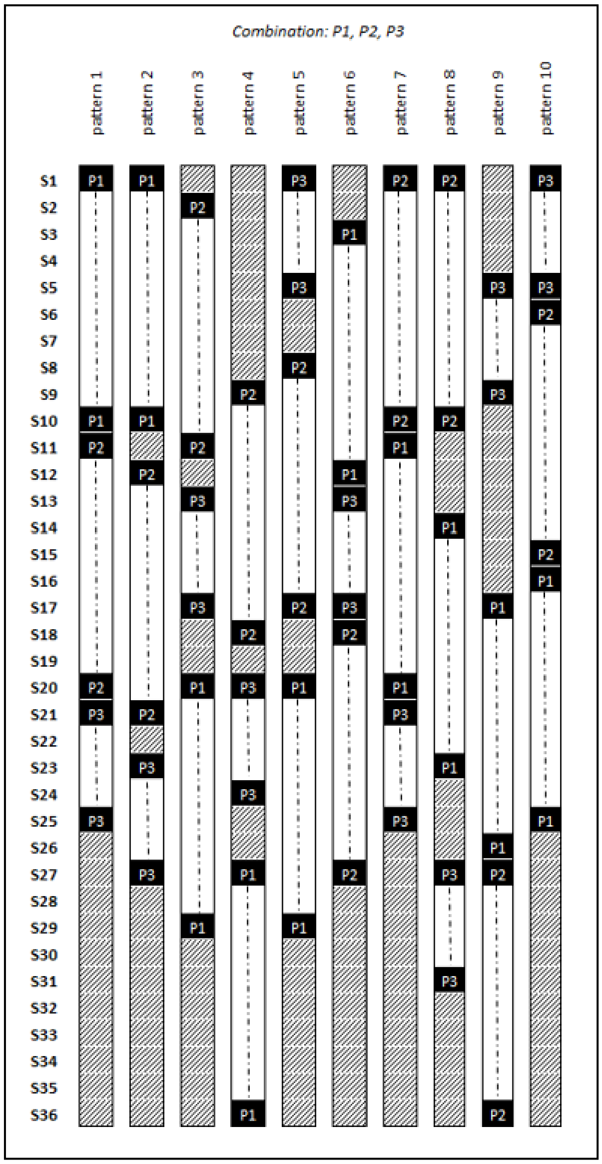

Figure 4: Possible patterns for the combination of patients P1, P2, P3. The hatched area corresponds to unused slots. P1 and P2 use 10 treatment slots, while P3 uses 5 slots.

Finally, to integrate the information of the patterns generated in a previous stage, the following parameters are defined:

- $A_{p,j}$ equals 1 if pattern p contains patient j.

- $I_{p,m}$ equals 1 if pattern p contains slot m as a start. A pattern includes one or more patients, all of them with different starting slots. Therefore, this parameter equals 1 as many times as there are patients contained in the pattern.
- $II_{j,p,m}$ equals 1 if given a patient j in particular, any pattern p contains that patient j, and also this patient begins its treatment in slot m.
- $F_{p,m}$ equals 1 if pattern p contains slot m as an ending. Under the same concept as parameter $I_{p,m}$, this parameter will equal 1 as many times as patients are in pattern p.
- H_p corresponds to the amount of extra hours associated with pattern p. In order to determine the value of this parameter, the difference between the finishing time of the last patient (according to what the pattern indicates) and the slot in which the working hours should finish has to be calculated. To consider extra hours in the modeling, the criteria by which patients are selected for a combination (see Table 1) must be modified, adding the extra hours to the whole duration of a workday.

Since treatment patterns contain the feasible sequence information in which a patient could be allocated to a chair, the problem is simplified to one of pattern allocation to treatment chairs. Nonetheless, it is also necessary to incorporate the lab dimension to the model, for which the following variables of binary decisions are defined:

- $x_{p,s,t}$ = equals 1 if pattern p is assigned to chair s on day t.

- $y_{j,m,t}$ = equals 1 if the patient j's medication is prepared during slot m on day t. The preparation of a medication may last longer than one slot. In this case, once the chemist starts to prepare it, it does not stop until it is finished. Thus, this variable will equal 1 for a same patient, for a certain amount of consecutive slots, so as to assign the necessary amount of preparation slots.

By using patterns the restrictions of a sequencing and allocation model are reduced to two. The first one corresponds to the allocation of every patient to a treatment chair (see Eq. 1); the second one, ensures that every chair has just one pattern associated to it, since each pattern describes the complete sequence of care, for a day, for any chair (see Eq. 2). Finally, because patients are treated in chairs that work in parallel, and since there is a fixed amount of nurses, we must consider the restriction stipulating that in every moment of time the amount of patients requiring care cannot exceed the total amount of nurses NE (see Eq. 3). The moments in which a patient requires care are when they begin their treatment and when it finishes. During the process it is assumed that the patient is sit in a treatment chair and there is no nurse care required.

$$Eq.1:\ \sum_{s\epsilon S}\ \sum_{p\epsilon P:\,A_{p,j}=1} x_{p,s,t} = 1 \qquad \forall\, j\epsilon\, J, t\,\epsilon\, T$$

$$Eq.2:\ \sum_{p\in P} x_{p,s,t} \leq 1 \qquad \forall\, s\,\epsilon\, S, t\,\epsilon\, T$$

$$Eq.3:\ \sum_{s\epsilon S}\ \sum_{\substack{p\epsilon P:\\ (I_{p,m}=1\ or\ F_{p,m}=1)}} x_{p,s,t} \leq NE \qquad \forall\, m\,\epsilon\, M, t\,\epsilon\, T$$

To prepare the medication, there are three conditions that constrain the problem, and that determine the sequencing of patients. The first one (see Eq. 4), is to allocate the medication preparation hours of every patient to some of the lab slots available. This restriction does not consider a specific sequence for the modules corresponding to every patient *j*, it just verifies that the total amount of slots required from the lab does not exceed the available capacity of it. The left side of the equation considers possible the medication preparation of a patient the day before (first component of the sum), or the same day (second component of the sum).

The second restriction considered is that all the necessary slots to prepare the medication of patient *j* must be allocated before it starts its treatment (see Eq. 5). This is the condition that relates the lab availability with the allocation of patients to chairs (understanding the allocation as determining a sequence and starting slots), and that constrains the hour in which a patient can start its treatment in case its treatment requires its medication to be prepared the same day. The left side of the restriction ensures that $y_{j,m,t}$ will equal 1 if there is availability of lab, and also if patient *j* has not been allocated to start its treatment before slot *m*. Finally, a restriction is added, which ensures that a medication will not be prepared in two consecutive days (see Eq. 6).

$$Eq. 4:\ \sum_{m \epsilon M} (y_{j,m,t-1})(1-\alpha_j) + \sum_{m \epsilon M} y_{j,m,t} = QL_j \qquad \forall\, j \epsilon\, J, t\, \epsilon\, T$$

$$Eq. 5:\ (1-\beta_{t,m})(1 - \sum_{k:k\leq m} II_{j,p,k} \sum_{s \epsilon S} x_{p,s,t}) \leq\ y_{j.m.t} \quad \forall\, m\, \epsilon\, M, t\, \epsilon\, T, p\, \epsilon\, P, j\, \epsilon\, J\ :\ A_{p,j} = 1$$

$$Eq. 6:\ y_{j,m,t} \leq 1 - \frac{\sum_m y_{j,m,t-1}}{H} \qquad \forall\, m\, \epsilon\, M, j\, \epsilon\, J, t\, \epsilon\, T\ \ and\ H \gg 1$$

Lastly, in order to determine the optimum solution of the problem, an objective function was defined that minimizes the amount of extra hours in which every treatment chair incurs. This ensures that each treatment chair is assigned a pattern that allows the completion of patient care as soon as possible (which is the objective of a traditional machine-programming model). Gathering all the elements, the entire scheduling model obtained is as follows:

$$min \sum_{t \in T} \sum_{s \epsilon S} \sum_{p \epsilon P} H_p x_{p,s,t}$$

subject to:

$$\sum_{s \epsilon S} \sum_{p \epsilon P:\, A_{p,j}=1} x_{p,s,t} = 1 \quad \forall j \epsilon J, t \epsilon T$$

$$\sum_{p \in P} x_{p,s,t} \leq 1 \quad \forall\, s \epsilon S, t \epsilon T$$

$$\sum_{s \epsilon S} \sum_{\substack{p \epsilon P: \\ (I_{p,m}=1 \text{ or } F_{p,m}=1)}} x_{p,s,t} \leq NE \quad \forall\, m \epsilon M, t \epsilon T$$

$$\sum_{m \epsilon M} (y_{j,m,t-1})(1-\alpha_j) + \sum_{m \epsilon M} y_{j,m,t} = QL_j \quad \forall\, j \epsilon J, t \epsilon T$$

$$(1-\beta_{t,m})(1 - \sum_{k:k \leq m} II_{j,p,k} \sum_{s \epsilon S} x_{p,s,t}) \leq \; y_{j,m,t} \quad \forall\, m \epsilon M, t \epsilon T, p \epsilon P, j \epsilon J \;:\; A_{p,j} = 1$$

$$y_{j,m,t} \leq 1 - \frac{\sum_m y_{j,m,t-1}}{M} \quad \forall\, m \epsilon M, j \epsilon J, t \epsilon T \text{ and } M \gg 1$$

$$x_{p,s,t} \epsilon \{0,1\} \qquad \forall p \epsilon P, \; s \epsilon S, t \epsilon T$$

$$y_{j,m,t} \epsilon \{0,1\} \qquad \forall j \epsilon J, \; m \epsilon M, t \epsilon T$$

2.5. Case Study Characterization

The performance of the proposed methodology will be evaluated for the case of an oncology unit, which has a staff of one oncologist, three nurses, and seven treatment chairs. Figure 5 shows the demand distribution for seven months of the medical consultations record, where we can highlight that the 56% of the treated patients, during that period, present colon cancer. In the same vein of Figure 5, Table 2 shows information concerning the entry of new patients to the system. Of the total of patients, the 69% corresponds to new patients (patients who enter the system between January and July, 2015), and this percentage is similarly maintained if the analysis per cancer type is disaggregated. With the information of new patients given by the hospital it is possible to build the rate of entries to the Chemotherapy Unit of new patients per cancer type (see Table 2), data needed in order to implement the posed methodology in previous sections.

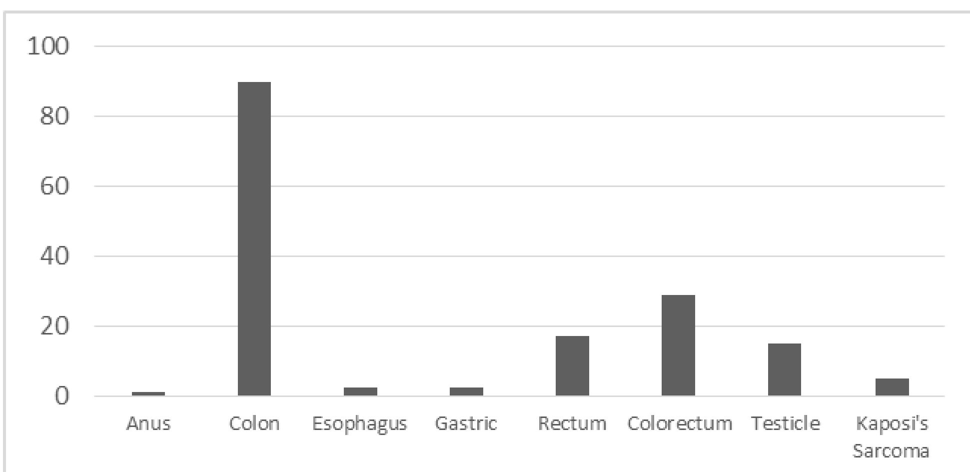

Figure 5: Number of patients per cancer type treated in the Chemotherapy Unit between January and July 2015

Table 2: Characterization of the demand of patients, from the Chemotherapy Unit, treated between January and July 2015

Cancer type	*N° of patients*	*% of total*	*N° of new patients*	*Arrival rate [requests/day]*
Anus	1	0,62%	1	0,005
Colon	90	55,90%	62	0,425
Esophagus	2	1,24%	1	0,009
Gastric	2	1,24%	1	0,009
Rectum	17	10,56%	12	0,080
Colorectum	29	18,01%	20	0,137
Testicle	15	9,32%	10	0,071
Kaposi's Sarcoma	5	3,11%	3	0,024
TOTAL	161	100%	111	0,760

Regarding the treatments, there are currently 55 chemotherapy protocols. Among these protocols, 21 correspond to cancer types that have patients' records. In order to group the protocols we categorized them per cancer type and then determined based on the information contained in the protocol, the amount of total slots that each treatment requires and the amount of sessions that a patient must undergo according to the protocol (see Table 3). It is noteworthy that some treatments present the exact same structure (total amount of slots, sessions, and cycle length); however, they differ from each other in the medication that must be given to the patient. In Table 3, this can be observed in the testicular cancer case (protocols 35 and 36) and in the colorectal cancer one (protocols 37 and 39).

Nowadays, the method used by the hospital to schedule the patients is the following. Every week, the medical committee approves the patients who will undergo chemotherapy. Once these patients are ready to start their treatment, they are ordered according to a priority established by medical criteria, and they are scheduled in this order, on Mondays or Wednesdays, depending on the availability of time slots. That is to say, the first patients are allocated on Monday, until there is no more capacity, and then, the scheduling continues on Wednesday. If there is not enough space to allocate the patients, these could be delayed until their deadline, after which they will have to be scheduled in extra hours.

Table 3: Characterization of protocols for chemotherapy treatments for different cancer types

Cancer type	*Treatment description*	*Capacity requirements*	*Sessions/Slots*
Testicle	Protocol 35	3x(5x22)	15/330
	Protocol 36	3x(5x22)	15/330
Colon	Protocol 12	6x(5x11)	30/330
Colorectal	Protocol 11	4x25	4/100
	Protocol 26	12x15	12/180
	Protocol 37	8x12	8/96
	Protocol 39	8x12	8/96
Rectal	Protocol 38	1x1	1/1
Gastric	Protocol 15	4x9 + 3x9	7/63
	Protocol 18	6x23	6/138
	Protocol 19	4x(21) + 4x(4x17)	20/356
	Protocol 23	4x21	4/84
	Protocol 27	6x(5x9)	30/270
Anal	Protocol 01	1x5 + 1x4	2/9
	Protocol 02	1x31 + 1x29	2/60
	Protocol 32	1x5 + 1x5	2/10
Kaposi's Sarcoma	Protocol 09	7x6	7/42
Esophagus	Protocol 13	1x13 + 3x27 + 1x13 + 3x27	8/178

Table 4, shows for every cancer type, the maximum amount of days that a patient's beginning of a treatment could be delayed. The priority of each cancer type is stipulated by medical criteria, and considers three factors: if the patient is GES (Health Explicit Guarantees, priority established by the Health Ministry) or not, urgency level of the patient (where 2 is very urgent and 0 not very urgent), and improvement possibilities (where 2 is a high probability of improvement and 0 low or null). The priority score for every cancer type is calculated by adding these four parameters. It is important to mention that both the scoring scales and the method to calculate the priority were established along with the Chemotherapy team since, currently, there is no formal method to calculate this prioritization.

Table 4: Patient prioritization according to cancer type

Cancer Type	*Maximum Delay [days]*	*Priority*	*Justification*			
			GES	*Urgency*	*Recovery posibilities*	*Total*
Testicle	7	1	1	2	2	5
Colon	7	2	1	1	1	3
Colorectal	7	3	1	1	1	3
Rectal	7	4	1	1	1	3
Gastric	28	5	0	1	1	2
Kaposi's Sarcoma Anal	14	6	1	0	0	1
Esophagus	14	7	0	0	0	0

Regarding the daily scheduling of patients, today the Chemotherapy Unit has two time blocks of patient care for treatment sessions. The first one, from 8 AM to 12 PM, and the second one, from 2 PM to 5 PM. For every day there is a list of patients that must be treated, and the head nurse determines in which chair and time slot each patient will begin its treatment, depending on the available space. If a patient's treatment is extended beyond the length of the first time block, a corresponding chair is blocked for the rest of the day, and no other patient can use it afterwards.

2.6. Results

The scheduling of patients in time, which corresponds to the first part of the addressed problem, was programmed in Microsoft Visual Studio 14.0.23107.156, both for the current hospital method and for the methodology adapted from Sauré et al. (2012). The pattern generation for the patient scheduling was also done in Microsoft Visual Studio 14.0.23107.156, while the subsequent mathematical model was programmed in GAMS 23.5, using CPLEX as a solver.

In order to implement the first part of the methodology, it is necessary as a first step to group the chemotherapy treatments according to their similar structure features. This, in order to perform the patient categorization and prioritize them later. Based on the information contained in Table 3, some protocols were grouped by similarity, such as the case of protocols 35 and 36 for testicular cancer, or protocols 37 and 38 for colorectal cancer. Afterwards, the more frequent treatments in the patients' records given by the hospital, for each type of cancer, were selected, and around 11 groups or types of patients were finally determined (see Table 5). It is noteworthy that there may be more than one group for one type of cancer, such as the case of groups 3, 4, and 5 that indicate colorectal cancer for a patient, but differ in their treatment structure. On the other hand, for the case of gastric cancer, the opposite situation occurs, since there are just five protocols but only one group associated with this cancer. This is because all the patients presented the structure described by protocol 23, in the patient care record.

From the data showed in Table 5, we generated the arrival of patients per cancer type following a Poisson distribution (see Sauré et al. 2012). Afterwards, both scheduling methodologies were programmed, using the same generated patients database. In order to compare the performance of both of them, we performed a simulation that considered a booking horizon of 300 days and a planning horizon of 1000 days. Also, a period of warm up of 300 days was considered to evaluate the methodology in a state of regime (non-empty calendar). We ran 100 replicas and for each one of them the performance indicators defined were measured: delayed patients percentage (DPP), extra consultation slots used (ECS), and extra treatment slots used (ETS).

Table 5: Treatment groups used to evaluate the proposed methodology

Type	*Capacity requirements*	*Sessions/slots*	*Arrival rate [reqs./day]*	*Cancer*
1	3x(5x22)	15/330	0,071	Testicle (GES)
2	6x(5x11)	30/330	0,425	Colon (GES)
3	4x25	4/100	0,034	Colorectal (GES)
4	8x12	8/96	0,068	Colorectal (GES)
5	12x15	12/180	0,034	Colorectal (GES)
6	1x1	1/1	0,080	Rectal (GES)
7	4x21	4/84	0,009	Gastric
8	1x5 + 1x5	2/10	0,002	Anal
9	1x31 + 1x29	2/60	0,003	Anal
10	7x6	7/42	0,024	Kaposi's Sarcoma
11	1x13 + 3x27 + 1x13 + 3x27	8/178	0,009	Esophageal

Table 6 shows the results obtained after the simulation. For the metric DPP, it can be seen that in the hospital's case, from the 100 replicas made, in 43 of them between a 10% and a 20% of the patients were delayed, on average; while the posed methodology delayed more frequently, between a 40% and a 50% of the patients on average (63% of the replicas). Regarding metric ECS, in 46% of the replicas the amount of extra slots of medical consultation used, on average, was between 0.6 and 0.7 daily slots (that is, between 9 and 11 minutes); while with the posed methodology, in 48% this value was maintained between 0.5 and 0.6 slots (between 7, 5, and 9 minutes). Finally, for metric ETS is can be observed that for the case of the hospital 39% of the replicas required from 5 to 10 extra treatment slots (1.25 to 3 hours), daily, on average; while with the posed methodology this proportion was greater (53% of the replicas).

Table 6: Simulation results

	Frecuency			*Frecuency*			*Frecuency*	
DPP	*Hospital*	*Methodology*	*ECS*	*Hospital*	*Methodology*	*ETS*	*Hospital*	*Methodology*
< 10%	**34**	0	<0,1	0	0	<5	1	7
10%- 20%	**43**	0	0,1 - 0,2	0	0	5 - 10	39	**53**
20% - 30%	16	1	0,2 - 0,3	0	0	10 - 15	**34**	26
30% – 40%	6	**27**	0,3 - 0,4	0	2	15 - 20	24	12
40% - 50%	0	**63**	0,4 - 0,5	5	**20**	20 - 25	1	2
50% – 60%	1	9	0,5 - 0,6	**29**	**48**	25 - 30	1	0
60% - 70%	0	0	0,6 - 0,7	**46**	**25**	30 <	0	0
70% – 80%	0	0	0,7 - 0,8	19	5			
80% - 90%	0	0	0,8 - 0,9	1	0			
90% <	0	0	0,9 <	0	0			

Regarding the number of patients whose treatments' start were delayed, the hospital's method presents a smaller average percentage than the one obtained with the suggested methodology. This is due to the short-sighted approach used in Chemotherapy in order to schedule the patients, in which they are scheduled as soon as they arrive, and therefore, there are only a few cases in which patients are delayed. The suggested methodology, instead, aims to book care modules in the future. Thus, around a 45% of the patients are delayed to the maximum waiting time allowed.

It is important to note that the fact that the suggested method presents a higher DPP does not imply that its performance is low, since there is no explicit penalty for delaying the beginning of a patient's treatment within the allowed range. The method posed by Sauré et al. (2012) does consider a penalty for delayed days, which is implicit in the policy proposed.

The method suggested presents a saving in the amount of extra hours used in comparison with the method currently used by Chemotherapy. For the case of extra medical consultations slots (ECS) the amount of extra care slots is less than 1 on average, for every replica. It follows that, currently, the care capacity on behalf of the oncologist is appropriate.

On the other hand, the number of extra slots intended for chemotherapy treatments (ETS) are not enough to fulfill the current demand. For this simulation, the hospital's method has an average daily deficiency of 14±5 treatment slots (or 3.4±1.2 treatment hours), while the proposed method presents a deficiency of 11±4 treatment slots (or 2.8±1.2 hours). It is noteworthy that this results does not imply that the workday needs an extension of 3 hours, but rather that around 3 extra care hours are required, which could be effectuated in a parallel manner. Finally, the amount of extra consultation slots for a year was 378±47 (or 94±12 hours) and 333± 50 (or 83±12 hours) on average, for the hospital and the posed method, respectively; whereas the amount of extra treatment slots for a year was of 8,194±3,045 (or 2,048±761 hours) and 6,789± 2,939 (or 1,697±735 hours), on average. Using the proposed method, instead of the current methodology used in Chemotherapy, would allow saving a 20% of costs per extra hour.

In order to implement the second part of the methodology, which corresponds to the daily patient scheduling, a calendar was made for one year, using the proposed method. Due to the high demand for colon cancer treatments (see Table 5), the calendar obtained presents a structure of similar weeks. That is to say, weeks in which there is a specific demand profile composed mainly by colon cancer patients. These profiles may slightly vary, due to the randomness of the patients' arrivals, but in general they present a configuration that is cyclically repeated in time. Figure 6, shows a standard demand profile for any week. It can be observed that for weeks 1 and 5 the demand for treatment slots is practically identical, where all the patients demanding 11 treatment slots correspond to colon cancer patients. To determine the performance of the mathematical model suggested, we solved the problem for a week that presents a profile which repeats in time. In this case, week 5 was chosen.

For the chosen week, 83,195 patterns were generated in total, in a time inferior to 2 minutes. These patterns were cleaned, in order to remove those options that are not frequently used in practice. For example, an allocation for a chair with just one patient who starts its treatment session at the end of the day, or cases with more than three patients per chair[3]. After removing these type of cases, the number of patterns in total for the week is 10,834. With this amount of patterns, it is possible to obtain an optimal solution for the

3 Given the treatment structures and average session duration (11 slots), in most cases it is not possible to schedule more than 3 patients in the same treatment chair.

problem, in just a few seconds; while with a traditional model (that is, without using patterns), it was not possible to obtain a solution, due to the lack of computational memory. The computer used to generate the patterns and solving the model was a 2.2 gigahertz Quad Core PC (processor Intel ® Core ™ i7-5200U) with 8 gigabytes of RAM.

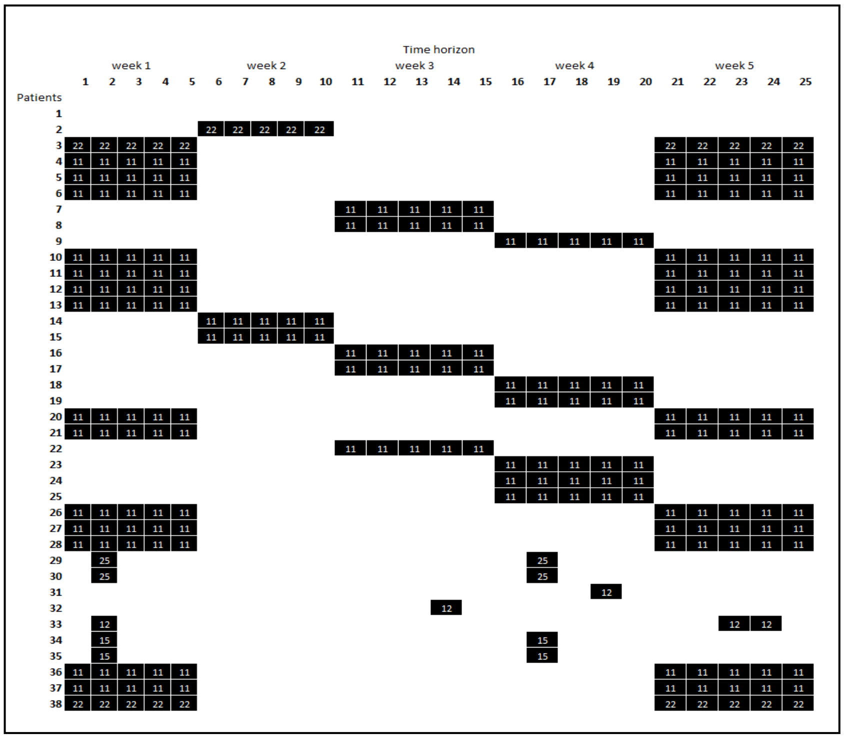

Figure 6: Extract of the generated calendar from the Sauré et al. (2012) method

Figure 7 a) shows the optimal solution obtained with the mathematical model and Figure 7 b) shows the solution that would be obtained with the method used by the Chemotherapy Unit today, both for the day with greatest demand in the week. The method currently used by the hospital consists of two time blocks in which the patients' sessions are allocated. If a session lasts longer than block 1's duration (in this case, patients P3 and P8), the chair will be blocked for the rest of the day, impeding other patients to receive their treatments in the same chair.

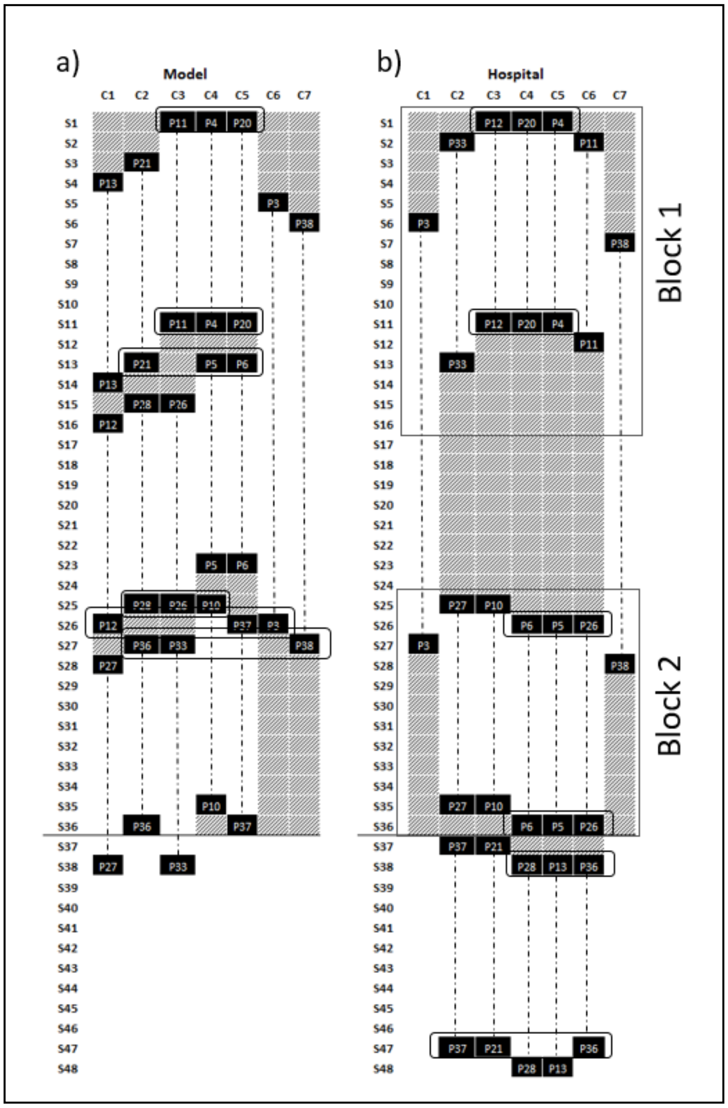

Figure 7: Results of the allocation of patients to treatment chairs, for a Thursday of a standard week. The hatched area represents the treatment slots not used. The working day ends in slot 36, all the subsequent slots correspond to extra hours.

Table 7 contains the solution for two scenarios using the hospital and the proposed methods. The results obtained in both scenarios, where Scenario 1 presents a normal demand of patients and Scenario 2 a critical situation with a high demand of patients[4], show that the policy of fixed time blocks established by the hospital constrains the

4 To define a critical day, 21 colon cancer patients (each one of them requiring 11 care modules) were estimated as a maximum. Assuming a maximum of 3 patients per treatment chair, and a total of 7 chairs, this configuration is tight

solution, which results in a significant loss of care capacity. The number of slots not used for patient care in the hospital Scenario 1 was 21% greater than the results obtained using our methodology, which implies that the proposed method manages a more efficient use of care capacity than the current hospital method. Thus, due to a better capacity management the proposed model achieves to serve the last patient 10 slots (2.5 hr) earlier than the hospital method and incurs in 83.3% less extra care hours.

Regarding the use of lab hours, in Scenario 1 the hospital's method achieves a 22% less capacity usage in the day than our method and incurs in more extra lab hours the previous day, because in the hospital scenario patients with preparation constraints are scheduled early in the morning, therefore, their medication must be prepared the previous day. The extra hours needed should be externalized with an additional cost associated, which was not considered within the objective function of the model, since we assumed that it is not possible for the hospital to increase the lab's capacity.

Table 7: Optimization results for daily patient scheduling

		Chemotherapy Unit				*Laboratory*	
		FTLP [slot]	*EST [slots]*	*Number of patients using extra slots*	*Care Capacity Loss*	*Same Day Lab Capacity Usage*	*Previous Day Exceeding Slots*
Scenario 1:	Hospital Method	48	12	5	40%	64%	14
Normal day	Proposed Method	38	2	2	19%	86%	11
Scenario 2:	Hospital Method	49	68	8	32%	75%	60
Congested day	Proposed Method	46	18	4	12%	100%	58

enough to need extra hours. For the generated calendar, this demand profile is found among the 10 profiles that are frequently obtained.

It is important to mention that the capacity use depends strongly on the number of patients whose medication must be prepared the same day. That is to say, if a large number of patients of this type arrive, the difference between the optimal solution and the one provided by the hospital's method would not be significant, since the solution tends to be just one: use the same day all the available lab slots for patients whose medication must be prepared that day, and use the available hours of the previous day to prepare the medication of the rest of the patients.

An important analysis based on these results is how different trade-offs perform considering different resources. In the example shown in Figure 7, the solution obtained by our model provides a low use of extra hours (4 care slots) given the demand of patients. However, in days in which this demand is greater, it is interesting to study the possibility of requiring extra resources, whether treatment chairs or nurses.

From the calendar generated through simulation, a categorization of the daily capacity use was made (in amount of care slots required), and based on this, we identified 24 demand configurations which will inevitably result in the use of a significant amount of extra hours (critical days) and which represent the 11% of all the scheduled days. From the critical days generated, the scheduling was made for a day in which 21 patients arrive, who require 11 care slots, and two cases were evaluated: i) allow the use of extra hours, and ii) do not allow the use of extra hours, but consider the option of adding extra treatment chairs, if necessary.

We used the configuration of Scenario 2 (see Table 7) to evaluate each case. The optimal solution found for the first case considers a workday that finishes 2.5 hours after the regular working hours, and also, that incurs in the use of 16 extra care slots. On the other hand, the results for the second case provide an optimal scheduling that requires increasing in 2 the provision of treatment chairs in order to reach a feasible solution, and thus, achieve to treat all the patients. In case ii) the 2 extra treatment chairs added enable to treat 4 patients, who in case i) are treated in a workday 2.5 hours longer, in which two more nurses are required to work in parallel. The trade-off between the acquisition of 2 extra treatment chairs and hiring 5 extra care hours of clinical nurses encourages the option of allowing overtime in the workday. It is important to highlight that this analysis also depends in the proportion of the critical cases that may occur. As it was mentioned before, the current demand of patients generated contains an 11% of critical cases. However, if the demand increases in the future and the resources available today remain constant, there will be a moment when the cost of hiring overtime for every critical day that occurs will be inferior to acquiring extra treatment chairs.

Finally, we analyzed the impact of adding one more nurse for case i), in which the use of extra hours is allowed. With this measure, it was possible to reduce in two slots the extra care capacity needed. Nonetheless, the additional extension of the workday did not suffer any changes, since it was not possible to relocate the entire session of a patient within the working hours. The addition of one more nurse does not have a significant impact in the reduction of the overtime cost, since a sufficient saving of care slots for a whole treatment session (which usually lasts several hours) is not achieved.

2.7. Conclusions

This paper describes a methodology to address the scheduling problem of chemotherapy patients, which is divided in two stages: the first one consists in scheduling the medical appointments and treatment sessions of every patient throughout a time horizon; while the second one, addresses the daily scheduling of patients. In order to address the patient scheduling throughout a time horizon, we adapted the policy established by Sauré et al. (2012) for radiotherapy treatments, which indicates the prioritization levels of the patients and how these should be scheduled according to features of their treatments. Regarding the second problem of patient scheduling, a two-part approach was proposed, which considers the generation of treatment patterns and also, a mathematical model for pattern allocation that incorporates restrictions of nurse care capacity and care hours available in the lab. The methods can be applied in practice with the objective of reducing the functioning costs incurred by the Chemotherapy Unit, ensuring the compliance of medical standards of patient care.

The results of this work show that for the first stage of the problem the scheduling policy implemented overcomes the current method used by the hospital to schedule patients. Regarding the costs' impact, the method proposed in this paper manages to reduce in a 20% the operational costs of the hospital, due to less extra treatment hours needed.

On the other hand, the proposed daily scheduling method for patients presents an improvement of 21% in care slots usage and 22% in lab slots usage for an average demand day with respect to the current methods applied to the use of resources. This translates in a reduction of both extra hours used and workday duration. The solutions of both stages of the posed methodology were obtained at a resolution time of seconds (or minutes for certain cases of pattern generation), which implies that the developed method is applicable in practice, and it would allow real improvements in the Chemotherapy Unit functioning.

This work does not explicitly include waiting costs of patients due to the delay in their treatments' starts, since the policy of Sauré et al. (2012) already includes this cost in the problem modeling. Therefore, when implementing the policy, the cost of delaying a patient is implicitly considered. Regarding the daily scheduling of patients, an aspect to emphasize is that since the data of all patients was no available, it is not possible to conclude whether an additional nurse is needed. Although there was no major impact observable when increasing to 1 de current staff of nurses, the effect may be different if the demand is greater, since the restriction of not treating a certain number of patients in a parallel manner would be an active restriction, turning into a bottleneck. The last issue to consider is related to the case in which it is possible to allocate more than 3 patients in a treatment chair, since the amount of generated patterns increases exponentially and complicates the computational implementation. Therefore, for these cases, it will be necessary to consider more efficient methods for scheduling, or pattern generation.

Further work extensions consider alternative schedules for laboratory dedication to the preparation of medication, in order to measure the impact of the daily patient scheduling, including the randomness of medication preparation times and the daily no-show factor. Also, it could be considered in further work to incorporate the clinical nurses intervention in several opportunities during a session, and not only at the beginning and end of it. Finally, there may be incorporated mixed treatments in the future, in which a combination of chemotherapy and radiotherapy are required, which implies the consideration of a new significant restriction of resource compatibility.

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ANNEXES

ANNEX A : PAPER SENT TO EUROPEAN JOURNAL OF OPERATIONAL RESEARCH

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Title: Appointment Scheduling and Patient Programming in Chemotherapy: A Case Study in a Chilean Hospital

Article Type: Innovative Application of OR

Section/Category: (O) OR in health services

Keywords: Health Care; Scheduling; Chemotherapy; Appointment

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Abstract: This research addresses a scheduling problem for chemotherapy patients, which is divided in two subproblems: patient scheduling on an infinite horizon and daily patient scheduling. We consider the requirement for available lab hours to prepare the medicine for every patient as an additional complexity. A methodology was formulated that addresses the problem in two stages. The first one is based on previous research and implements a scheduling policy for chemotherapy. The result of this first stage is the input for the second stage, which is addressed by generating treatment patterns. The benefits of both stages of the proposed methodology are evaluated for a real case. Regarding the costs' impact, the method proposed manages to reduce 20% the operational costs of the hospital, due to less extra treatment hours needed. On the other hand, the proposed daily scheduling method for patients presents an improvement of 21% in care slots usage and 22% in lab slots usage for an average demand day, which translates in a reduction of both extra hours used and workday duration.

Appointment Scheduling and Patient Programming in Chemotherapy: A Case Study in a Chilean Hospital

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Highlights for: Appointment Scheduling and Patient Programming in Chemotherapy: A Case Study in a Chilean Hospital

- We solve a problem that considers patient scheduling through a time horizon and patient programming for a specific day.
- The resources we worked with are treatment chairs, medical care hours and laboratory hours.
- The problem is solved in two stages, the first one with a stochastic dynamic programming approach and the second one using an optimization model.
- Patients programming is modeled as a parallel machine optimization problem and the high combinatorial is addressed using patterns of information.
- We solve the problem for a real case in a public hospital in Santiago, Chile. The method proposed shows better performance indicators than the current method used by the hospital.

Appointment Scheduling and Patient Programming in Chemotherapy: A Case Study in a Chilean Hospital

Abstract

This research addresses a scheduling problem for chemotherapy patients, which is divided in two subproblems: patient scheduling on an infinite horizon and daily patient scheduling. We consider the requirement for available lab hours to prepare the medicine for every patient as an additional complexity. A methodology was formulated that addresses the problem in two stages. The first one is based on previous research and implements a scheduling policy for chemotherapy. The result of this first stage is the input for the second stage, which is addressed by generating treatment patterns. The benefits of both stages of the proposed methodology are evaluated for a real case. Regarding the costs' impact, the method proposed manages to reduce 20% the operational costs of the hospital, due to less extra treatment hours needed. On the other hand, the proposed daily scheduling method for patients presents an improvement of 21% in care slots usage and 22% in lab slots usage for an average demand day, which translates in a reduction of both extra hours used and workday duration.

Keywords: Health Care, Scheduling, Chemotherapy, Appointment.

1. Motivation

The problem that this investigation addresses is the one faced today by the Unit of Chemotherapy at the Salvador Hospital, in Santiago of Chile. The scheduling of chemotherapy patients may consider two dimensions: the scheduling of sessions in an infinite horizon, and the daily scheduling of patient care.

Concerning the first dimension, it is required that the sessions follow the predetermined structure for the treatment to be effective. Hence, once the appointment is scheduled, it is not possible to change it in case there is no medical capacity to treat the patient. This implies that it is possible that there is no allocation of patients, whose treatments fit perfectly and no modules are lost (Sauré et al., 2012). Furthermore, there are some types of cancer with a higher priority care than others, whether for urgency, speed of disease development, or for improvement possibility.

The second dimension presents two challenges. Firstly, each chemotherapy treatment uses a determined quantity of limited resources: hours spend in a treatment chair, considering both oncologists and nurses. An important aspect to consider is the impact of the laboratories operations in the daily management of chemotherapy patients. The laboratory has limited time capacity, aimed to prepare the hospital's orders, which constrains how patients should be managed on a daily basis. The second challenge is the complexity of the problem structure itself. The daily scheduling of patients is categorized as a parallel machine programming problem, which is NP-complete (Du and Leung, 1990) and must be solved for numerous parallel machines; this implies an extensive associated combinatorial.

Nowadays, the methodology used by the Unit of Chemotherapy consists in the use of extra hours of care, and postponing the beginning of certain patients' treatment. This is due not only to the lack of care capacity, but also it is the outcome of an unplanned management of care hours, nurses shifts and treatment chair hours. The costs of not having a proper scheduling of patients is monetary, as it implies and extra expense for the hospital to supplement the lack of capacity with extra hours; as well as social, as certain patients have to delay their treatment start due to the lack of capacity.

There are publications available in literature, which state that a delay in the treatment initiation of a patient has detrimental effects in their chances of survival, either because there is a progress in the development of the tumors, or because the symptoms worsen rapidly over time (Ragaz et al., 2005). This happens, for example, in patients with testicular or colon cancer, where both diseases are quite frequent, and develop rapidly over time (O'Rourke and Edwards, 2000; Chen et al., 2008; Sauré et al., 2012; Song et al., 2013; McLaughlin et al., 2012; Bos et al., 2015; Bernard and Sweeney, 2015). Therefore, relying on a formal, efficient, and robust methodology that allows the scheduling of patients and plan the daily health care is essential in order to decrease the extra expense of the Unit of Chemotherapy.

This paper is organized as follows. In Section 2 a collection of related literature with this research is presented; in Section 3 we present a detailed description of chemotherapy treatments, session scheduling, and daily schedule of patients. In Section 4, two methodologies are described, so as to approach the two stages of the problem to be solved; then, in Section 5, the study of the Salvador Hospital case is characterized. In Section 6, the main results, a comparison of the proposed methodology with the one used at the hospital, and a sensitivity analysis of the main resources are presented. Finally, in Section 7, the main conclusions and future work are included.

2. Literature Review

This research focuses on the scheduling of chemotherapy treatments and addresses two main issues: the scheduling of patients through time and the daily scheduling of these patients' care services. The first issue refers to the allocation of medical hours or treatment sessions in a time horizon. Within the available techniques to solve scheduling problems, dynamic scheduling considers variables that are subject to random events and it has been used to address problems not only in healthcare. For example, it has been used in the industrial sector to solve staff planning problems (Ernst et al., 2004) and in the airline industry to determine commercial flights itineraries (Warburg et al., 2008; Jiang and Barnhart, 2009). In healthcare, this method has been used to coordinate the daily allocation of medical resources to patients in a clinic (Gupta and Denton, 2008), to schedule medical care and treatments for patients with different care priorities (Patrick et al., 2008; Sauré et al., 2012) and to schedule patients considering no-show (Liu et al., 2010).

The second issue that this research approaches refers to the daily scheduling of patients. The problem the hospital has to solve corresponds to a machine programming problem with parallel machines, dependent on each other, where the objective is to minimize the moment in which the last patient ends its treatment. Among the existing works we can mention Yalaoui and Chu (2002), who solved the machine-programming problem in parallel through a Branch and Bound algorithm, Anghinolfi and Paolucci (2007) who present a hybrid metaheuristic which combines Tabu Search and Simulated Annealing and Li et al. (2011), who suggest different theoretical approaches to the solution and a heuristic based on Simulated Annealing. Other authors that suggest the implementation of heuristics in order to solve the machine-programming problem are Bilge et al. (2004). Between the publications available in the literature, it was not possible to find any in which the programming of machines model was used in order to solve the patients scheduling problem.

Literature referring to the scheduling of cancer treatments (both chemotherapy and radiotherapy) is divided into two currents of thought: one that approaches the problem in a static manner and another one that solves the problem in a dynamic manner. In the static problem, the scheduling choices are made at the beginning of the evaluation period.

The dynamic one refers to the methods used for scheduling appointments for patients before they set a day for their treatments, when the demand is yet uncertain.

Among the publications that address the scheduling problem in a static manner, the work of Conforti et al. (2008) can be found, who propose a mathematical model to solve a radiotherapy session scheduling problem. The authors consider a base case in which the calendar does not contain previously scheduled patients. Later, they pose an extension in which it is consider the case where the system does not start empty and allows rescheduling patients that were previously scheduled. The authors also made an extension of this publication, in which they consider priorities for patients and a block of flexible duration length (Conforti et al., 2010).

Petrovic and Leite-Rocha (2008) address the radiotherapy-scheduling problem as well, and they consider two rules for scheduling: forward and backward. The former refers to begin scheduling patients from their waiting deadlines, while the latter refers to scheduling patients as they enter the system. This research aims to establish rules or policies that enable scheduling in an easy and rapid manner, without impairing the quality of the solution. Among recent publications that aim for this type of perspective, Patrick et al. (2008) and Sauré et al. (2012) can be mentioned, who pose scheduling policies under a dynamic approach. Both publications consider an infinite horizon, multiple priorities, and the use of overtime.

The scheduling of chemotherapy treatments may address not only the scheduling of sessions, but also the manner in which these patients must be treated daily. A work already available in literature, which considers both stages, is the Condotta and Shakhlevich (2014) one. They not only schedule patients in a finite horizon, but they also determine the sequence of activities for the personnel during the day. However, unlike our research, the authors consider a static approach for scheduling the patients' sessions, and they do not include in the daily timetabling the use of laboratory capacity for the medication preparation.

In the same vein of daily patient scheduling, the work of Le et al. (2015) can be mentioned, who solve the scheduling problem of hematology and chemotherapy treatments. For this, the authors propose a mathematical model first and a Tabu Search heuristic in a second stage. The problem solved by the authors considers a static scheduling, in which the treatment sessions of the patients are allocated together, disregarding the uncertain future demand. The problem solved by the authors considers a static scheduling, in which the treatment sessions of the patients are allocated together, disregarding the uncertain future demand. The problem solved aims to optimize the allocation of the nurses' workload, and disregards the required time for the medication preparation for the patients, two issues that differ from the approach proposed in this paper.

3. Problem Definition

3.1. Characterization of Chemotherapy Treatments

A chemotherapy treatment is composed by a determined amount of sessions, in which the patient is provided with a specific combination of medication. These sessions have a defined length, which may vary according to the treatment or even for a same treatment, and are held throughout a time horizon according to a cycle that could be every month or every two weeks, for example. The established structure for the treatment should be respected in order for the treatment to be effective, therefore, it is not possible to reschedule sessions if there is no capacity for a certain day.

For each session (or set of sessions corresponding to one week) the patient must be treated firstly with the treating oncologist, who requests for an examination in order to validate that the patient is in condition to receive a treatment. Therefore, every time a cycle begins an hour for medical consultation is also needed.

3.2. Available resources

The Chemotherapy Unit is composed by one oncologist, three clinical nurses who are in charge of executing the treatments, and seven treatment chairs. The oncologist works twice a week, has a care capacity of 36 slots of 15 minutes each, and the average length of a consultation corresponds to two slots (30 minutes). Each clinical nurse and treatment chair is available for 36 slots every day. The lab receives preparation orders for a certain day until the previous day at midday. It also dedicates a number of time slots in the morning to prepare the medication that requires to be made during the same day.

3.3. Patient scheduling on an infinite horizon

Patients arrive randomly to the Chemotherapy Unit and have to go through a previous process in order to start its treatment, which may take one or several sessions with the treating oncologist. This research will not include this stage, and the entry day of a patient to the system will be considered as the day in which all the previous stages of treatment approval are already done.

Since the treatments have a fixed structure that indicates the amount of sessions and the gap between them, the decision is when each patient starts its treatment. This depends on the available capacity of (i) time slots for patient care (medical attention) and (ii) time slots for patient care in every treatment chair. It is noteworthy that for every type of cancer there is a maximum time stipulated to postpone the start of a patient's treatment, due to the rapid development of cancer. Furthermore, every type of cancer has a priority level assigned under medical criteria, which considers factors such as the severity of the disease, improvement probabilities, and additional constraints established by the Ministry of Health. Therefore, the timetabling must respect this prioritization when allocating patients throughout the time horizon.

Example 1. Consider a small example of 10 patients arriving to the system throughout one month. In Figure 1 two timetables can be observed, where the upper one corresponds to the patient care scheduling (oncologist session), and the lower one to the treatment sessions. Each row corresponds to the timetable of one patient, and the hatched area indicates weekend days in which there is no patient care. The arrival day of each patient to the system is known (stuck blocks), and based on this information a medical appointment is scheduled with the treating oncologist, starting from the week after its entry (see upper timetable). There are cases in which the patient may be delayed beyond the week after its entry, such as the case of patients P2 and P8. Patient P2 enters during the first week, however, its first session is scheduled for the third week. Likewise, patient P8 enters the third week, but the start of its treatment is postponed at least two weeks. These delays are due to the non-existing capacity of patient care for a consultation to take place prior to the session the week after the patient's entry. It can be observed that the lower timetable structure, corresponding to the treatment sessions, depends on the scheduling with the oncologist.

In order to measure the impact of the scheduling decisions, three metric units were established: Delayed Patients Percentage (DPP), Extra Consultation Slots (ECS), and Extra Treatment Slots (ETS). The first metric is related to patient's service level regarding waiting times to begin their treatment. The second and third metrics allow the quantification of missing capacity. The final result of this first stage is the allocation of patients to their

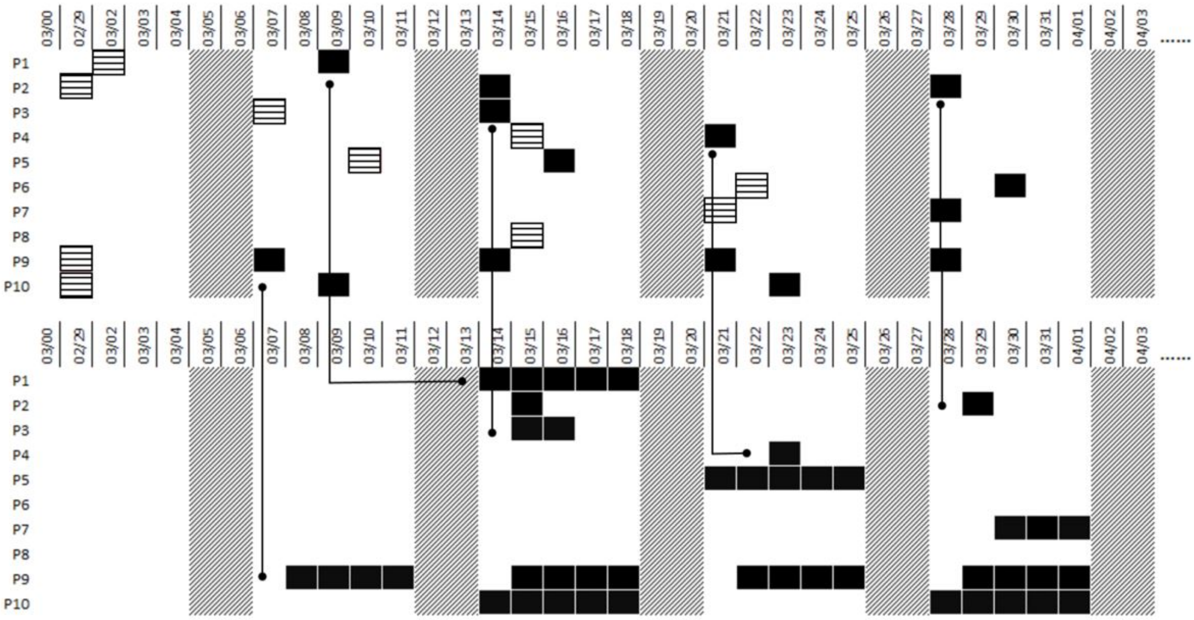

Figure 1: Example of the arrival and scheduling of medical appointments of patients for a month of the time horizon.

first day of treatment, and therefore, since there is a specific protocol for every patient that defines the treatment structure, the complete agenda of the sessions for each patient is determined.

3.4. Daily patient scheduling

The procedure used by the hospital in order to achieve a daily planning begins with deciding which patients will be treated in each treatment chair and when. Once this allocation has been done, there is a list of tasks per chair, determined by the treatments of the corresponding patients. This list of tasks is assigned to the clinical nurses, which results in a sequence of daily tasks for every nurse. It is noteworthy that, as a general rule, if a nurse starts treating a patient, it must perform all the stages of the treatment that correspond to that patient. However, in the case of the hospital where this research was conducted, it is allowed for a patient to be treated by more than one nurse.

A further significant condition that is considered in this research is the laboratory service capacity. The lab can prepare the medication for one day on the afternoon of the day, or the same day in the morning. Also, certain slots of the previous day in the morning could be used, if they are available and there is lack of capacity. In case all the available capacity of the lab is used, the preparation of the medication will be externalized to another lab, which implies an additional cost for the hospital.

Example 2. Figure 2 shows a scheduling of patients for a random day in Chemotherapy. Diagram a) shows a timetable for 13 patients, of whom only two (P3 and P10) require their medication prepared the same day. For this example, 3 clinical nurses were considered, and the slots in which the resource nurse is used at full capacity can be observed in the diagram. The hatched area corresponds to the patient care time that was not used. Given the characteristics of the treatments and the restriction of not exceeding a maximum of nurses, it is not possible to distribute the patients in a way that they fit perfectly and no slots are lost during the day. Diagram b) shows the lab hours used the day before (left scheduling) and for the same day (right scheduling) of these same patients. The example considers for day n a lab capacity of 2 hours (8 slots) in the morning of the n and $n-1$ days, and 4 hours in the afternoon (16 slots) for day $n-1$. It is possible to see that all the lab slots of both mornings are completely used, and that day $n-1$ in the afternoon is collapsed, which implies externalizing the medication preparation to another lab for patients P12, P26 and P11. Furthermore, it is possible to see, in case there is available capacity in the morning of day n, that it is not possible to reschedule any patient (in this case, P6 and P26 cannot be treated the day before, because there would not be time to prepare their medication), which reflects that deciding at which time to schedule each patient, regarding the lab restrictions, is not trivial.

In order to measure the impact of the proposed method two metric were determined: finishing time of the last patient (FTLP), and extra slots used in order to treat the patients (EST). The former is related to the number of extra hours incurred by the Chemotherapy Unit, while the latter indicates the amount of extra capacity (in care slots) needed so extra hours are not required.

4. Solution Approach

4.1. Dynamic patient scheduling

In order to schedule the patients throughout a time horizon and determine the days in which they have to attend to a session, we implemented the model posed by Sauré et al. (2012). This method solves a scheduling problem of radiotherapy patients through the formulation of a Markovian Decision Process, which considers an infinite horizon, multiple appointments, sessions of diverse lengths, and the use of overtime.

The methodology the authors proposed aims to minimize three components: cost of

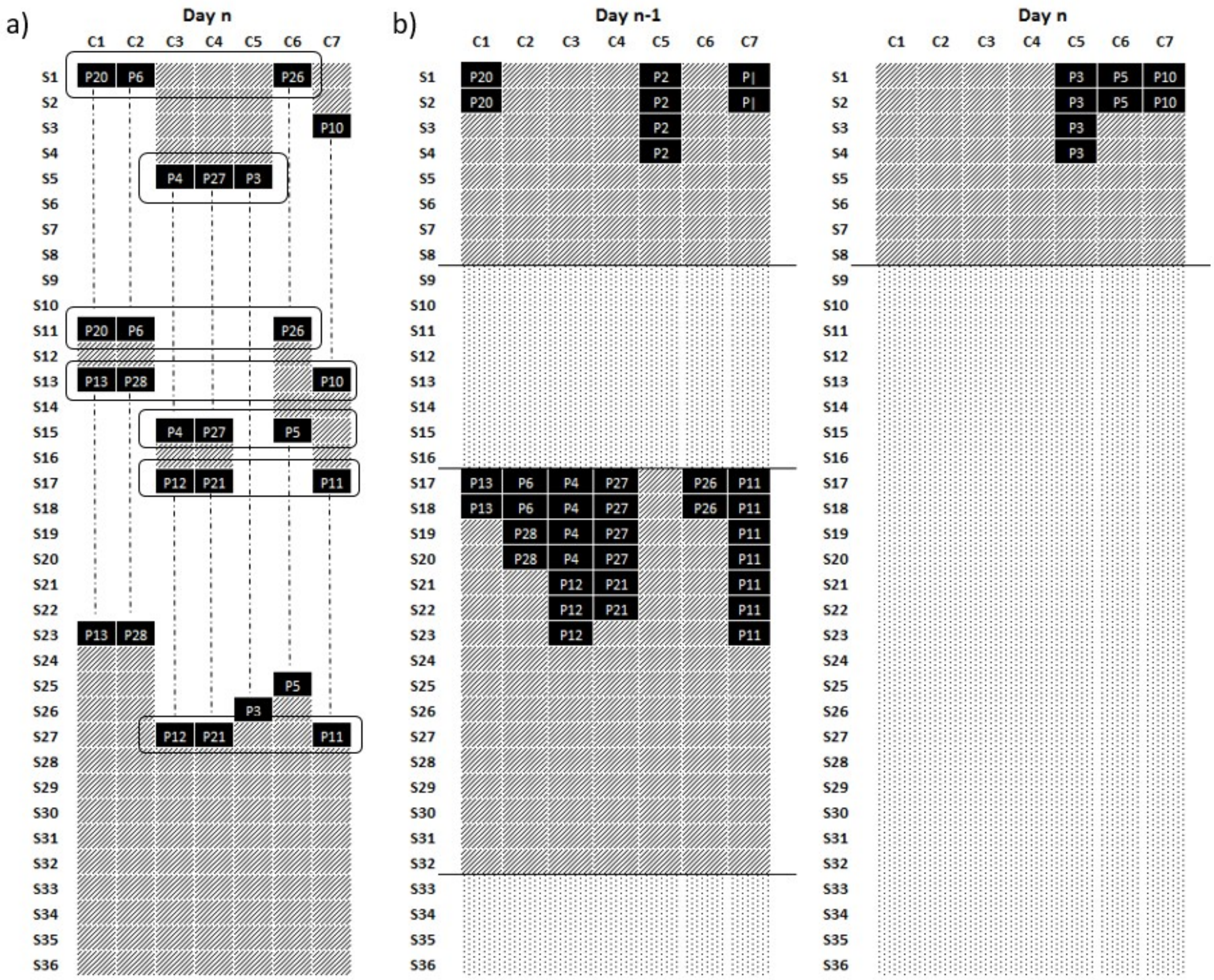

Figure 2: Example of the arrival and scheduling of medical appointments of patients for a month of the time horizon.

starting a treatment a certain day, cost of overtime usage, and cost of delaying the scheduling of a certain type of treatment. The method allowed the identification of the following scheduling policies for radiotherapy treatments: (a) schedule the greatest amount of demand the first day available, and the rest starting since their deadlines for beginning their treatments, (b) the greater the number of sessions, the earlier treatment should be scheduled, (c) those treatments with shorter sessions should be scheduled further in the future, and (d) the more urgent treatments, or with fewer time allowed to begin, should be scheduled as soon as possible.

As it was mentioned in Section 3, since radiotherapy and chemotherapy treatments consider in their structures the same conditions (in fact, radiotherapy treatments are a particular case of chemotherapy), the arrival of patients to the system in both cases behaves according to a Poisson process, and since Salvador Hospital considers the same costs to decide how to schedule the patients, it is possible to adapt the policy posed by Sauré et al. (2012) to chemotherapy treatments.

In order to implement the scheduling policy, it is necessary to define a category for the diverse treatments that the hospital currently has. This categorization is done based on the similarities of treatment structures, which include the amount of slots, cycle length, number of sessions and their durations. Once the treatments are grouped by type, two parameters must be established: booking horizon, which corresponds to the time horizon in which patients will be scheduled; and planning horizon, which corresponds to the whole time horizon in which patients will be scheduled. The planning horizon should consider at least the number of days as the booking horizon, plus the days of the longest treatment. That is to say, the most extreme case is considered, in which a patient with the more extensive treatment has its first sessions the last day of the booking horizon. Once the patients' categories and the time horizons are defined, the scheduling suggested by Sauré et al. (2012) is conducted as follows:

Step 1. Register the patients' arrival in one week. The patient scheduling will be conducted the last working day of a week.

Step 2. Order the patients in a queue considering the following elements, prioritizing according to the mentioned order: medical criteria (urgency and improvement possibility, established by the hospital), waiting time allowed (lesser time, greater priority), number of sessions (greater number of sessions, higher priority), and length of sessions (greater session length, higher priority). Thus, if there are two patients, one with a maximum waiting time of 14 days and 10 treatment sessions, and another one with a waiting time of 7 days and 8 sessions, the latter should be scheduled before, in spite of its smaller number of sessions, due to its shorter waiting time allowed.

Step 3. First, allocate the patient care hours starting from the first patient in queue. The first patient should be allocated in the first slot available, and so on, until there are no more available slots in the week.

Step 4. Allocate the rest of the patients starting from their deadlines.

Step 5. Considering the patient care allocation, distribute each patient's treatment hours. Each session can only be scheduled from the day after the consultation, and must be allocated within the same week of that consultation.

This scheduling policy differs from the one currently used by the hospital, since the latter conducts a short sighted allocation. That is to say, the medical appointments are scheduled according to patient arrival and no further capacity is booked in advance. However, it is important to highlight that in both cases there is a prioritization of patients, but in the hospital's case this is only based on medical criteria (urgency and improvement possibility). When implementing this scheduling policy, two calendars are obtained. One contains the days when each patient must attend to a medical appointment, and the other one indicates which days correspond to a session. This information is an input for the second stage of this methodology.

4.2. Pattern generation for the daily scheduling of patients

The daily scheduling of patients consists in determining a care order for a list of patients who have to be treated on the same day. This care order indicates in which treatment chair each patient has to receive its treatment and in which time slot. Therefore, for each chair a sequence of patients, who have to undergo chemotherapy sessions of varying length and different medical requirements, is determined. Treatment chairs work in parallel, so it is possible for several patients to be treated simultaneously, as far as there are available nurses. Finally, every treatment session specifies a time for the preparation of medication that could be produced during the day before or the same day in the morning. This time determines the possible time slots for a patient to start its treatment.

The decisions that have to be made present a challenge from the computational capacity viewpoint that is needed in order to solve the problem to optimality. In Example 2, which considers 7 treatment chairs, 14 patients during the day and 36 slots, the number of variables that indicate the allocation of patients, as well as the sequence in which they should be treated, is 9,359, and the number of corresponding restrictions is close to 78,403. An example of this dimension could be solved in a considerable time (more than one day) if there was a significant computational capacity, which is not applicable to the hospital's situation, as they have to solve this problem on a daily basis. Given the complexity of the problem structure, which presents a combinatorial nature that rapidly grows if more patients, chairs, or slots are considered, it is necessary to propose a new methodology to solve the problem.

We define treatment patterns in order to address the problem. A pattern corresponds to a possible allocation of patients to any chair, in which the sequence of patients and the slot in which they will start their treatments is indicated. To construct the patterns it is necessary to know what patients will be treated that day and how many slots their respective sessions require; information that is already known since it is the result of solving the previous scheduling problem (see subsection 4.1). Then, it is possible to determine all the feasible combinations (or groups) of patients for one treatment chair, which works a certain amount of slots per day (see Table 1). Once the feasible combinations for patients who can be allocated to one treatment chair have been determined, treatment patterns are generated on this basis. For each combination of patients there are multiple possibilities to place them in sequence. Moreover, the problem allows for these patients not to be necessarily treated consecutively. That is to say, each patient may begin its treatment considering a wide range of scheduling options. In order to build a pattern, all the possible permutations of a specific combination of patients for one chair must be listed.

Patient	Session duration (15 min)
P1	10
P2	10
P3	5
P4	11
P7	25
P9	10
P10	10
P11	10
P14	5
P15	11

Some feasible combinations	Patients	Total slots
Combinations 1	P1, P2, P3	25
Combinations 2	P9, P10, P11, P14	35
Combinations 3	P12	22
Combinations 4	P5, P6	34
Combinations 5	P13, P14	9
Combinations 6	P3, P8, P13, P14	16
Combinations 7	P7, P8	27
Combinations 8	P9, P10, P11	30
Combinations 9	P12, P4, P8	35
Combinations 10	none	0

Table 1: Generation of some feasible combinations on the basis of 15 patients for one treatment chair that works for 36 slots (9 hours), daily. The list of combinations presented does not contain all the feasible combinations, but it is possible to see that the only rule that must be met is that the whole sum of the modules should be smaller than the working time of a chair. Under this concept, the combination P9, P10, P11, P12 is not valid.

Example 3. Figure 3 shows 10 possible patterns for the combination P1, P2, P3. Every pattern indicates both the order in which the patients will be treated, and the slot in which each one begins its treatment. It is noteworthy that since each patient may start its treatment in different slots, the number of feasible permutations for each combination of patterns increases rapidly. For this example that considers only one combination (P1, P2 and P3), the amount of possible patterns is 20,956. If the example is considered for a day shown in Table 1, where there are 10 combinations, the amount of patterns for one day reaches 2,170,723. Therefore, for an example with a greater amount of combinations, the number of possible permutations easily reaches the million scale.

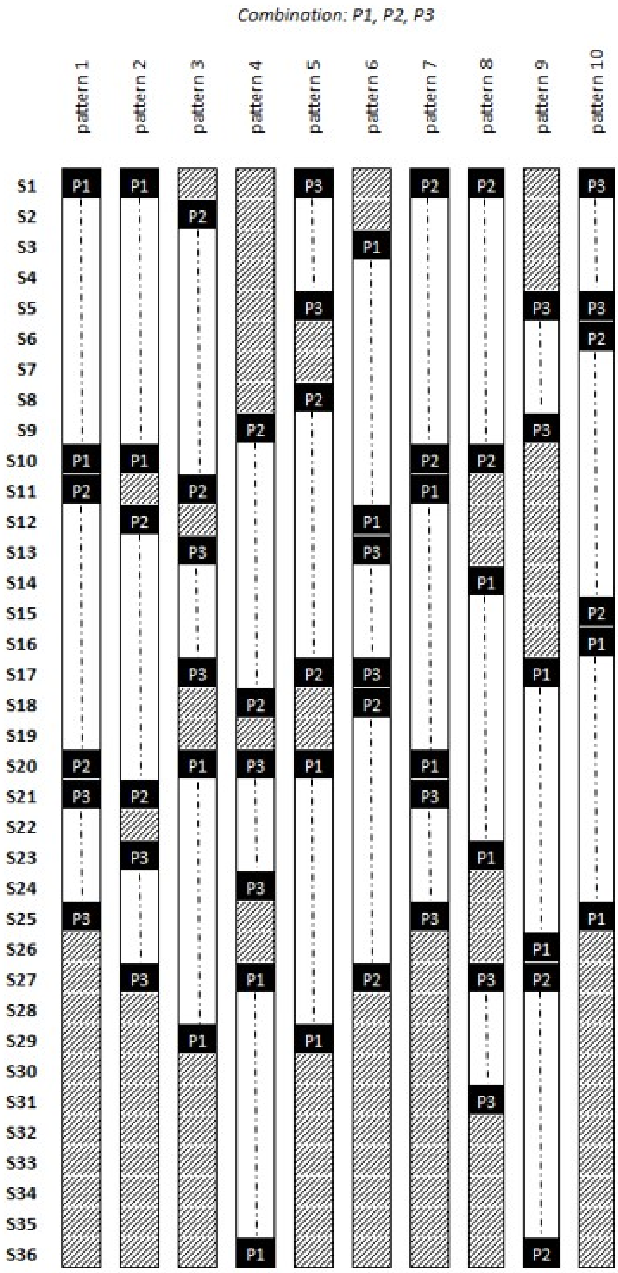

Figure 3: Possible patterns for the combination of patients P1, P2, P3. The hatched area corresponds to unused slots. P1 and P2 use 10 treatment slots, while P3 uses 5 slots.

4.3. Optimization model for the daily scheduling of patients

The mathematical model that corresponds to the problem of determining the order in which each patient will be treated in every chair, and the slot in which they start their treatment, combines two decisions: allocation of patients to chairs, and sequencing of patients in a treatment chair. These two decisions together generate an unmanageable combinatorial problem from a computational viewpoint. Building patterns allows to diminish the number of problem variables, since the possible sequences of patients are given to the model as an input, and the only decision left is whether to allocate each pattern to each treatment chair, in order to comply with the corresponding restrictions.

This problem considers a set of patients J who should be treated on day t. Each day is divided into a number of 15 minutes slots contained in set M. For every day there is a set of patterns P, which contains all the feasible allocation patterns for day t. Finally, sets S and T correspond to the amount of treatment chairs at disposal and the number of periods (days) for which a scheduling is required. In order to obtain the solution for a specific day, it is necessary to consider at least two periods of time, because while the patient care is during day t, there are lab slots of day $t-1$ in which the medication for day t might be prepared.

To consider the resources of the Chemotherapy Unit, the following parameters are defined:

NE : Corresponds to the number of nurses available for patient care.

β_{tm} : Binary parameter that equals 1 if the laboratory is busy during period t and slot m, and 0 otherwise.

QL_j : Indicates for every patient j how many lab slots are required to prepare the medication needed (information established in the corresponding treatment protocol).

α_j : Binary pattern that equals 1 if the medication of patient j has to be prepared the same day, and 0 otherwise.

Finally, to integrate the information of the patterns generated in a previous stage, the following parameters are defined:

A_{pj} : Binary parameters equals 1 if pattern p contains patient j.

I_{pm} : Binary parameter equals 1 if pattern p contains slot m as a start. A pattern includes one or more patients, all of them with different starting slots. Therefore, this parameter equals 1 as many times as there are patients contained in the pattern.

II_{jpm} : Binary parameter equals 1 if given a patient j in particular, any pattern p contains that patient j, and also this patient begins its treatment in slot m.

F_{pm} : Binary parameter equals 1 if pattern p contains slot m as an ending. Under the same concept as parameter I_{pm}, this parameter will equal 1 as many times as patients are in pattern p.

H_p : Corresponds to the amount of extra hours associated with pattern p. In order to determine the value of this parameter, the difference between the finishing time of the last patient (according to what the pattern indicates) and the slot in which the working hours should finish has to be calculated. To consider extra hours in the modeling, the criteria by which patients are selected for a combination (see Table 1) must be modified, adding the extra hours to the whole duration of a workday.

Since treatment patterns contain the feasible sequence information in which a patient could be allocated to a chair, the problem is simplified to one of pattern allocation to treatment chairs. Nonetheless, it is also necessary to incorporate the lab dimension to the model, for which the following variables of binary decisions are defined:

x_{pst} : Binary variable equals 1 if pattern p is assigned to chair s on day t.

y_{jmt} : Binary variable equals 1 if the patient j's medication is prepared during slot m on day t. The preparation of a medication may last longer than one slot. In this case, once the chemist starts to prepare it, it does not stop until it is finished. Thus, this variable will equal 1 for a same patient, for a certain amount of consecutive slots, so as to assign the necessary amount of preparation slots.

By using patterns the restrictions of a sequencing and allocation model are reduced to two. The first one corresponds to the allocation of every patient to a treatment chair (see Eq. (1)); the second one, ensures that every chair has just one pattern associated to it, since each pattern describes the complete sequence of care, for a day, for any chair (see Eq. (2)). Finally, because patients are treated in chairs that work in parallel, and since there is a fixed amount of nurses, we must consider the restriction stipulating that in every moment of time the amount of patients requiring care cannot exceed the total amount of nurses NE (see Eq. (3)). The moments in which a patient requires care are when they begin their treatment and when it finishes. During the process it is assumed that the patient is sitting on a treatment chair and there is no nurse care required.

$$\sum_{s \in S} \sum_{p \in P : A_{pj}=1} x_{pst} = 1 \;\; \forall j \in J, t \in T. \tag{1}$$

$$\sum_{p \in P} x_{pst} \leq 1 \;\; \forall s \in S, t \in T. \tag{2}$$

$$\sum_{s \in S} \sum_{p \in P : I_{pm}=1 \text{ or } F_{pm}=1} x_{pst} \leq NE \;\; \forall m \in M, t \in T. \tag{3}$$

To prepare the medication, there are three conditions that constrain the problem, and that determine the sequencing of patients. The first one (see Eq. (4)), is to allocate the medication preparation hours of every patient to some of the lab slots available. This restriction does not consider a specific sequence for the modules corresponding to every patient j, it just verifies that the total amount of slots required from the lab does not exceed the available capacity of it. The left side of the equation considers possible the medication preparation of a patient the day before (first component of the sum), or the same day (second component of the sum).

The second restriction considered is that all the necessary slots to prepare the medication of patient j must be allocated before it starts its treatment (see Eq. (5)). This is the condition that relates the lab availability with the allocation of patients to chairs (understanding the allocation as determining a sequence and starting slots), and that constrains the hour in which a patient can start its treatment in case its treatment requires its medication to be prepared the same day. The left side of the restriction ensures that y_{jmt} will equal 1 if there is availability of lab, and also if patient j has not been allocated to start its treatment before slot m. Finally, a restriction is added, which ensures that a medication will not be prepared in two consecutive days (see Eq. (6)).

$$\sum_{m \in M} y_{jmt-1}\,(1-\alpha_j) + \sum_{m \in M} y_{jmt} = QL_j \;\; \forall\, j \in J, t \in T. \tag{4}$$

$$(1-\beta_{tm})\left(1 - \sum_{k \in M: k \geq m} \sum_{s \in S} x_{pst}\right) \leq y_{jmt} \;\; \forall\, m \in M, t \in T, p \in P, j \in J : A_{pj} = 1. \tag{5}$$

$$y_{jmt} \leq 1 - \frac{\sum_{k \in M} y_{jk(t-1)}}{H} \;\; \forall\, m \in M, j \in J, t \in T, \text{ and } H \gg 1. \tag{6}$$

and we consider the conditions of the nature of the variables:

$$x_{pst} \in \{0,1\} \;\; \forall p \in P, s \in S, t \in T. \tag{7}$$

$$y_{jmt} \in \{0,1\} \;\; \forall j \in J, m \in M, t \in T. \tag{8}$$

Lastly, in order to determine the optimum solution of the problem, an objective function was defined that minimizes the amount of extra hours in which every treatment chair incurs. This ensures that each treatment chair is assigned a pattern that allows the completion of patient care as soon as possible (which is the objective of a traditional machine-programming model). Gathering all the elements, the entire scheduling model obtained is as follows:

$$\min \sum_{t\in T}\sum_{s\in S}\sum_{p\in P} H_p x_{pst} \tag{9}$$

subject to: (1)-(8)

5. Case Study Characterization

The performance of the proposed methodology will be evaluated for the case of an oncology unit, which has a staff of one oncologist, three nurses, and seven treatment chairs. In the Table 2 shows the demand distribution for seven months of the medical consultations record, where we can highlight that the 56% of the treated patients, during that period, present colon cancer and the information concerning the entry of new patients to the system. Of the total of patients, the 69% corresponds to new patients (patients who enter the system between January and July, 2015), and this percentage is similarly maintained if the analysis per cancer type is disaggregated. With the information of new patients given by the hospital it is possible to build the rate of entries to the Chemotherapy Unit of new patients per cancer type (see Table 2), data needed in order to implement the posed methodology in previous sections.

Cancer type	N^o of patients	% of total	N^o of new patients	Arrival rate [request/day]
Anus	1	0,62%	1	0,005
Colon	90	55,90%	62	0,425
Esophagus	2	1,24%	1	0,009
Gastric	2	1,24%	1	0,009
Rectum	17	10,56%	12	0,08
Colorectum	29	18,01%	20	0,137
Testicle	15	9,32%	10	0,071
Kaposi's Sarcoma	5	3,11%	3	0,024
TOTAL	161	100%	111	0,76

Table 2: Characterization of the demand of patients, from the Chemotherapy Unit, treated between January and July 2015.

Regarding the treatments, there are currently 55 chemotherapy protocols. Among these protocols, 21 correspond to cancer types that have patients' records. In order to group the protocols we categorized them per cancer type and then determined based on the information contained in the protocol, the amount of total slots that each treatment requires and the amount of sessions that a patient must undergo according to the protocol (see Table 3). It is noteworthy that some treatments present the exact same structure (total amount of slots, sessions, and cycle length); however, they differ from each other in the medication that must be given to the patient. In Table 3, this can be observed in the testicular cancer case (protocols 35 and 36) and in the colorectal cancer one (protocols 37 and 39).

Nowadays, the method used by the hospital to schedule the patients is the following. Every week, the medical committee approves the patients who will undergo chemotherapy. Once these patients are ready to start their treatment, they are ordered according to a priority established by medical criteria, and they are scheduled in this order, on Mondays or Wednesdays, depending on the availability of time slots. In other words, the first patients are allocated on Monday, until there is no more capacity, and then, the scheduling continues on Wednesday. If there is not enough space to allocate the patients, these could be delayed until their deadline, after which they will have to be scheduled in extra hours.

Table 4, shows for every cancer type, the maximum amount of days that a patient's beginning of a treatment could be delayed. The priority of each cancer type is stipulated by medical criteria, and considers three factors: if the patient is GES (Health Explicit Guarantees, priority established by the Health Ministry) or not, urgency level of the patient (where 2 is very urgent and 0 not very urgent), and improvement possibilities (where 2 is a high probability of improvement and 0 low or null). The priority score for every cancer type is calculated by adding these four parameters. It is important to mention that both the scoring scales and the method to calculate the priority were established along with the Chemotherapy team since, there is no formal method to calculate this prioritization.

Regarding the daily scheduling of patients, today the Chemotherapy Unit has two time blocks of patient care for treatment sessions. The first one, from 8 AM to 12 PM, and the second one, from 2 PM to 5 PM. For every day there is a list of patients that must be treated, and the head nurse determines in which chair and time slot each patient will begin its treatment, depending on the available space. If a patient's treatment is extended beyond the length of the first time block, a corresponding chair is blocked for the rest of the day, and no other patient can use it afterwards.

6. Results

The scheduling of patients in time, which corresponds to the first part of the addressed problem, was programmed in Microsoft Visual Studio 14.0.23107.156, both for

Cancer type	Treatment description	Capacity requirements	Sessions/Slots
Testicle	Protocol 35	$3 \times (5 \times 22)$	15/330
	Protocol 36	$3 \times (5 \times 22)$	15/330
Colon	Protocol 12	$6 \times (5 \times 11)$	30/330
Colorectal	Protocol 11	4×25	4/100
	Protocol 26	12×15	12/180
	Protocol 37	8×12	8/96
	Protocol 39	8×12	8/96
Rectal	Protocol 38	1×1	1/1
Gastric	Protocol 15	$4 \times 9 + 3 \times 9$	7/63
	Protocol 18	6×23	6/138
	Protocol 19	$4 \times 21 + 4 \times (4 \times 17)$	20/356
	Protocol 23	4×21	4/84
	Protocol 27	$6 \times (5 \times 9)$	30/270
Anal	Protocol 01	$1 \times 5 + 1 \times 4$	2/9
	Protocol 02	$1 \times 31 + 1 \times 29$	2/60
	Protocol 32	$1 \times 5 + 1 \times 5$	2/10
Kaposi's Sarcoma	Protocol 09	7×6	7/42
Esophagus	Protocol 13	$1 \times 13 + 3 \times 27 + 1 \times 13 + 3 \times 27$	8/18

Table 3: Characterization of protocols for chemotherapy treatments for different cancer types.

			Justification			
Cancer type	Maximum Delay [days]	Priority	GES	Urgency	Recovery possibilities	Total
Testicle	7	1	1	2	2	5
Colon	7	2	1	1	1	3
Colorectal	7	3	1	1	1	3
Rectal	7	4	1	1	1	3
Gastric	28	5	0	1	1	2
Kaposi's Sarcoma Anal	14	6	1	0	0	1
Esophagus	14	7	0	0	0	0

Table 4: Patient prioritization according to cancer type.

the current hospital method and for the methodology adapted from Sauré et al. (2012). The pattern generation for the patient scheduling was also done in Microsoft Visual Studio 14.0.23107.156, while the subsequent mathematical model was programmed in GAMS 23.5, using CPLEX as a solver.

In order to implement the first part of the methodology, it is necessary as a first step to group the chemotherapy treatments according to their similar structure features. This, in order to perform the patient categorization and prioritize them later. Based on the information contained in Table 3 of Section 5, some protocols were grouped by similarity, such as the case of protocols 35 and 36 for testicular cancer, or protocols 37 and 38 for colorectal cancer. Afterwards, the more frequent treatments in the patients' records given by the hospital, for each type of cancer, were selected, and around 11 groups or types of patients were finally determined (see Table 5). It is noteworthy that there may be more than one group for one type of cancer, such as the case of groups 3, 4, and 5 that indicate colorectal cancer for a patient, but differ in their treatment structure. On the other hand, for the case of gastric cancer, the opposite situation occurs, since there are just five protocols but only one group associated with this cancer. This is because all the patients presented the structure described by protocol 23, in the patient care record.

From the data showed in Table 5, we generated the arrival of patients per cancer type following a Poisson process. Afterwards, both scheduling methodologies were programmed, using the same generated patients database. In order to compare the performance of both of them, we performed a simulation that considered a booking horizon of 300 days and a planning horizon of 1,000 days. Also, a period of warm up of 300 days was considered to evaluate the methodology in a state of regime (non-empty calendar). We ran 100 replicas and for each one of them the performance indicators defined in Subsection 3.3 were measured: delayed patients percentage (DPP), extra consultation slots used (ECS), and extra treatment slots used (ETS).

Type	Capacity requirements	Sessions/Slots	Arrival rate [reqs./day]	Cancer
1	3x(5x22)	15/330	0,071	Testicle (GES)
2	6x(5x11)	30/330	0,425	Colon (GES)
3	4x25	4/100	0,034	Colorectal (GES)
4	8x12	8/96	0,068	Colorectal (GES)
5	12x15	12/180	0,034	Colorectal (GES)
6	1x1	1/1	0,080	Rectal (GES)
7	4x21	4/84	0,009	Gastric
8	1x5 + 1x5	2/10	0,002	Anal
9	1x31 + 1x29	2/60	0,003	Anal
10	7x6	7/42	0,024	Kaposi's Sarcoma
11	1x13 + 3x27 + 1x13 + 3x27	8/178	0,009	Esophageal

Table 5: Treatment groups used to evaluate the proposed methodology.

Table 6 shows the results obtained after the simulation. For the metric DPP, it can be seen that in the hospital's case, from the 100 replicas made, in 43 of them between a 10% and a 20% of the patients were delayed, on average; while the posed methodology delayed more frequently, between a 40% and a 50% of the patients on average (63% of the replicas). Regarding metric ECS, in 46% of the replicas the amount of extra slots of medical consultation used, on average, was between 0.6 and 0.7 daily slots (that is, between 9 and 11 minutes); while with the posed methodology, in 48% this value was maintained between 0.5 and 0.6 slots (between 7, 5, and 9 minutes). Finally, for metric ETS can be observed that for the case of the hospital 39% of the replicas required from 5 to 10 extra treatment slots (1.25 to 3 hours), daily, on average; while with the posed methodology this proportion was greater (53% of the replicas).

Regarding the number of patients whose treatments' start were delayed, the hospital's method presents a smaller average percentage than the one obtained with the suggested methodology. This is due to the myopic approach used in Chemotherapy in order to schedule the patients, in which they are scheduled as soon as they arrive, and therefore, there are only a few cases in which patients are delayed. The suggested methodology, instead, aims to book care modules in the future. Thus, around a 45% of the patients are delayed to the maximum waiting time allowed.

	Frequency			Frequency			Frequency	
DPP	Hospital	Methodology	ECS	Hospital	Frequency	ETS	Hospital	Methodology
<10%	**34**	0	<0.1	0	0	<5	1	7
10% - 20%	**43**	0	0.1 - 0.2	0	0	5 - 10	39	**53**
20% - 30%	16	1	0.2 - 0.3	0	0	10 - 15	**34**	26
30% - 40%	6	**27**	0.3 - 0.4	0	2	15 - 20	24	12
40% - 50%	0	**63**	0.4 - 0.5	5	**20**	20 - 25	1	2
50% - 60%	1	9	0.5 - 0.6	**29**	**48**	25 - 30	1	0
60% - 70%	0	0	0.6 - 0.7	**46**	**25**	30 <	0	0
70% - 80%	0	0	0.7 - 0.8	19	5			
80% - 90%	0	0	0.8 - 0.9	1	0			
90% <	0	0	0.9 <	0	0			

Table 6: Simulation results.

It is important to note that the fact that the suggested method presents a higher DPP does not imply that its performance is low, since there is no explicit penalty for delaying the beginning of a patient's treatment within the allowed range. The method posed by Sauré et al. (2012) does consider a penalty for delayed days, which is implicit in the policy proposed.

The method suggested presents a saving in the amount of extra hours used in comparison with the method currently used by Chemotherapy. For the case of extra medical consultations slots (ECS) the amount of extra care slots is less than 1 on average, for every replica. It follows that, currently, the care capacity on behalf of the oncologist is appropriate.

On the other hand, the number of extra slots intended for chemotherapy treatments (ETS) are not enough to fulfill the current demand. For this simulation, the hospital's method has an average daily deficiency of 14±5 treatment slots (or 3.4±1.2 treatment hours), while the proposed method presents a deficiency of 11±4 treatment slots (or 2.8±1.2 hours). It is noteworthy that this results does not imply that the workday needs an extension of 3 hours, but rather that around 3 extra care hours are required, which could be performed in a parallel manner. Finally, the amount of extra consultation slots for a year was 378±47 (or 94±12 hours) and 333±50 (or 83±12 hours) on average, for the hospital and the posed method, respectively; whereas the average amount of extra treatment slots for a year was of 8,194±3,045 (or 2,048±761 hours) and 6,789± 2,939 (or 1,697±735 hours), respectively. Using the proposed method, instead of the current methodology used in Chemotherapy, would allow saving a 20% of costs per extra hour.

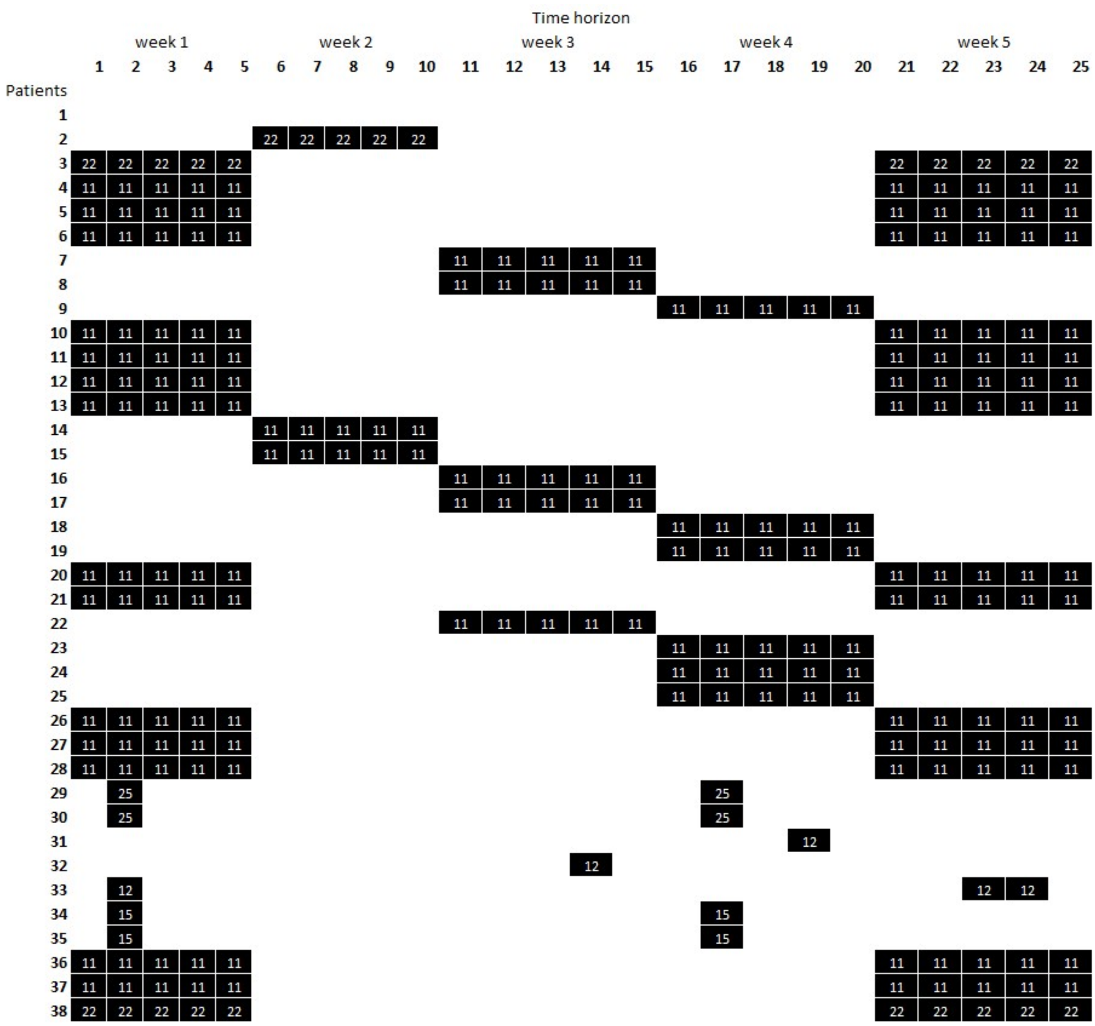

Figure 4: Extract of the generated calendar from the Sauré et al. (2012) method. The value in each cell indicates the amount of treatment modules necessary for one patient and day.

In order to implement the second part of the methodology, which corresponds to the daily patient scheduling, a calendar was made for one year, using the proposed method. Due to the high demand for colon cancer treatments (see Table 5), the calendar obtained presents a structure of similar weeks. That is to say, weeks in which there is a specific demand profile composed mainly by colon cancer patients. These profiles may slightly vary, due to the randomness of the patients' arrivals, but in general they present a configuration that is cyclically repeated in time. Figure 4, shows a standard demand profile for any week. It can be observed that for weeks 1 and 5 the demand for treatment slots is practically identical, where all the patients demanding 11 treatment slots correspond to colon cancer patients. To determine the performance of the mathematical model suggested, we solved the problem for a week that presents a profile which repeats in time. In this case, week 5 was chosen.

For the chosen week, 83,195 patterns were generated in total, in a time inferior to 2 minutes. These patterns were cleaned, in order to remove those options that are not frequently used in practice. For example, an allocation for a chair with just one patient who starts its treatment session at the end of the day, or cases with more than three patients per chair. After removing these type of cases, the number of patterns in total for the week is 10,834. With this amount of patterns, it is possible to obtain an optimal solution for the problem, in just a few seconds; while with a traditional model (that is, without using patterns), it was not possible to obtain a solution, due to the lack of computational memory. The computer used to generate the patterns and solving the model was a 2.2 gigahertz Quad Core PC (processor Intel Core i7-5200U) with 8 gigabytes of RAM.

Figure 5 a) shows the optimal solution obtained with the mathematical model and Figure 7 b) shows the solution that would be obtained with the method used by the Chemotherapy Unit today, both for the day with greatest demand in the week. The method currently used by the hospital consists of two time blocks in which the patients' sessions are allocated. If a session lasts longer than block 1's duration (in this case, patients P3 and P8), the chair will be blocked for the rest of the day, impeding other patients to receive their treatments in the same chair.

Table 7 contains the solution for two scenarios using the hospital and the proposed methods. The results obtained in both scenarios, where Scenario 1 presents a normal demand of patients and Scenario 2 a critical situation with a high demand of patients, show

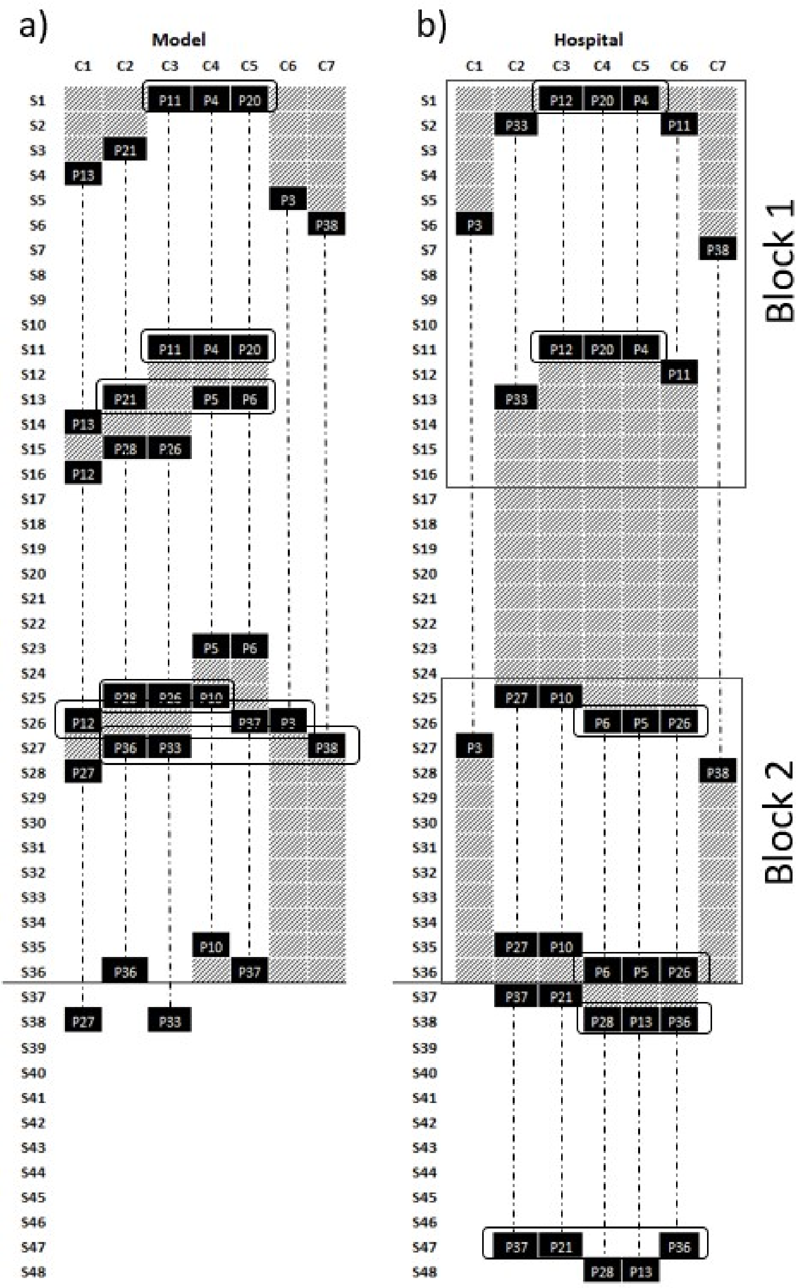

Figure 5: Results of the allocation of patients to treatment chairs, for a Thursday of a standard week. The hatched area represents the treatment slots not used. The working day ends in slot 36, all the subsequent slots correspond to extra hours.

that the policy of fixed time blocks established by the hospital constrains the solution, which results in a significant loss of care capacity. The number of slots not used for patient care in the hospital Scenario 1 was 21% greater than the results obtained using our methodology, which implies that the proposed method manages a more efficient use of care capacity than the current hospital method. Thus, due to a better capacity management the proposed model achieves to serve the last patient 10 slots (2.5 hr) earlier than the hospital method and incurs in 83.3% less extra care hours.

Regarding the use of lab hours, in Scenario 1 the hospital's method achieves a 22% less capacity usage in the day than our method and incurs in more extra lab hours the previous day, because in the hospital scenario patients with preparation constraints are scheduled early in the morning, therefore, their medication must be prepared the previous day. The extra hours needed should be externalized with an additional associated cost, which was not considered within the objective function of the model, since we assumed that it is not possible for the hospital to increase the lab's capacity.

				Chemotherapy Units		Laboratory	
		FTLP [slots]	EST [slots]	Number of patients using extra slots	Care capacity loss	Same day lab capacity usage	Previous day exceeding slots
Scenario 1: Normal day	Hospital Method	48	12	5	40%	64%	14
	Proposed Method	38	2	2	19%	86%	11
Scenario 2: Congested day	Hospital Method	49	68	8	32%	75%	60
	Proposed Method	46	18	4	12%	100%	58

Table 7: Optimization results for daily patient scheduling.

It is important to mention that the capacity used depends strongly on the number of patients whose medication must be prepared the same day. That is to say, if a large number of patients of this type arrive, the difference between the optimal solution and the one provided by the hospital's method would not be significant, since the solution tends to be just one: use the same day all the available lab slots for patients whose medication must be prepared that day, and use the available hours of the previous day to prepare the medication of the rest of the patients.

An important analysis based on these results is how different trade-offs perform considering different resources. In the example shown in Figure 5, the solution obtained by our model provides a low use of extra hours (4 care slots) given the demand of patients. However, in days in which this demand is greater, it is interesting to study the possibility of requiring extra resources, whether treatment chairs or nurses.

From the calendar generated through simulation, a categorization of the daily capacity used was made (in amount of care slots required), and based on this, we identified 24 demand configurations which will inevitably result in the use of a significant amount of extra hours (critical days) and which represent the 11% of all the scheduled days. From the critical days generated, the scheduling was made for a day in which 21 patients arrive, who require 11 care slots, and two cases were evaluated: (i) allow the use of extra hours, and (ii) do not allow the use of extra hours, but consider the option of adding extra treatment chairs, if necessary.

We used the configuration of Scenario 2 (see Table 7) to evaluate each case. The optimal solution found for the first case considers a workday that finishes 2.5 hours after the regular working hours, and also, that incurs in the use of 16 extra care slots. On the other hand, the results for the second case provide an optimal scheduling that requires increasing in two the provision of treatment chairs in order to reach a feasible solution, and thus, achieve to treat all the patients. In case (ii) the two extra treatment chairs added enable to treat four patients, who in case (i) are treated in a workday 2.5 hours longer, in which two more nurses are required to work in parallel. The trade-off between the acquisition of two extra treatment chairs and hiring five extra care hours of clinical nurses encourages the option of allowing overtime in the workday. It is important to highlight that this analysis also depends in the proportion of the critical cases that may occur. As it was mentioned before, the current demand of patients generated contains an 11% of critical cases. However, if the demand increases in the future and the resources available today remain constant, there will be a moment when the cost of hiring overtime for every critical day that occurs will be inferior to acquiring extra treatment chairs.

Finally, we analyzed the impact of adding one more nurse for case (i), in which the use of extra hours is allowed. With this measure, it was possible to reduce in two slots the extra care capacity needed. Nonetheless, the additional extension of the workday did not suffer any changes, since it was not possible to relocate the entire session of a patient within the working hours. The addition of one more nurse does not have a significant impact in the reduction of the overtime cost, since a sufficient saving of care slots for a whole treatment session (which usually lasts several hours) is not achieved.

7. Conclusions

This paper describes a methodology to address the scheduling problem of chemotherapy patients, which is divided in two stages: the first one consists in scheduling the medical appointments and treatment sessions of every patient throughout an infinite horizon; while the second one, addresses the daily scheduling of patients. In order to address the first stage, we adapted the policy established by Sauré et al. (2012) for radiotherapy treatments, which indicates the prioritization levels of the patients and how these should be scheduled according to features of their treatments. Regarding the second problem of patient scheduling, a two-part approach was proposed, which considers the generation of treatment patterns and also, a mathematical model for pattern allocation that incorporates restrictions of nurse care capacity and care hours available in the lab. The methods can be applied in practice with the objective of reducing the functioning costs incurred by the Chemotherapy Unit, ensuring the compliance of medical standards of patient care.

The results of this work, which are presented in Section 6, show that for the first stage of the problem the scheduling policy implemented overcomes the current method used by the hospital to schedule patients. Regarding the costs' impact, the method proposed in this paper manages to reduce in a 20% the operational costs of the hospital, due to less extra treatment hours needed.

On the other hand, the proposed daily scheduling method for patients presents an improvement of 21% in care slots usage and 22% in lab slots usage for an average demand day with respect to the current methods applied to the use of resources. This translates in a reduction of both extra hours used and workday duration. The solutions of both stages of the posed methodology were obtained at a resolution time of seconds (or minutes for certain cases of pattern generation), which implies that the developed method is applicable in practice, and it would allow real improvements in the Chemotherapy Unit functioning.

This work does not explicitly include waiting costs of patients due to the delay in their treatments' starts, since the policy of Sauré et al. (2012) already includes this cost in the problem modeling. Therefore, when implementing the policy, the cost of delaying a patient is implicitly considered. Regarding the daily scheduling of patients, an aspect to emphasize is that since the data of all patients was no available, it is not possible to conclude whether an additional nurse is needed. Although there was no major impact observable when increasing in one the current staff of nurses, the effect may be different if the demand is greater, since the restriction of not treating a certain number of patients in a parallel manner would be an active restriction, turning into a bottleneck. The last issue to consider is related to the case in which it is possible to allocate more than three patients in a treatment chair, since the amount of generated patterns increases exponentially and complicates the computational implementation. Therefore, for these cases, it will be necessary to consider more efficient methods for scheduling, or pattern generation.

Further work extensions consider alternative schedules for laboratory dedication to the preparation of medication, in order to measure the impact of the daily patient scheduling, including the randomness of medication preparation times and the daily no-show factor.

Also, it could be considered in further work to incorporate the clinical nurses intervention in several opportunities during a session, and not only at the beginning and end of it. Finally, there may be incorporated mixed treatments in the future, in which a combination of chemotherapy and radiotherapy are required, which implies the consideration of a new significant restriction of resource compatibility.

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