Interday and Intraday Chemotherapy Appointment Scheduling: a Patient-Centered Approach*

Giuliana Carello[a,*], Mauro Passacantando[b], Elena Tànfani[c]

[a] *Politecnico di Milano, Department of Electronics, Information and Bioengineering, piazza Leonardo da Vinci 32, Milan, 20133, Italy, giuliana.carello@polimi.it*

[b] *University of Milano-Bicocca, Department of Business and Law, via Bicocca degli Arcimboldi 8, Milan, 20126, Italy, mauro.passacantando@unimib.it*

[c] *University of Genova, Department of Economics, via Vivaldi 5, Genova, 16126, Italy, Elena.Tanfani@unige.it*

Abstract

The number of new cancer cases is expected to increase by about 50% over the next 20 years, and the need for chemotherapy treatments will increase accordingly. Treatments are usually provided in outpatient cancer centers, where patients with various types of cancers receive care. The treatment delivery must be carefully planned to optimize the use of limited resources, such as consultation and examination rooms, chairs and beds for the drug infusion, medical and nursing staff. The planning and scheduling of chemotherapy treatments involve different problems at different decision levels. In this work, we focus on the operational level and jointly address the interday and intraday multi-appointment scheduling problem. We determine the day and start time of the oncologist visit and drug infusion for a set of patients to be scheduled along a short-term planning horizon. We use a per-pathology policy, where the days of the week on which patients can be treated, depending on their pathology, are known. We consider different metrics that take into account the perspectives of both the cancer center and the patients. We formulate the problem as a multi-objective optimization problem, which is tackled by sequentially solving three problems in a lexicographic multi-objective fashion. The problems turn out to be computationally challenging; thus, we propose ad hoc decomposition approaches. The approaches are tested on real data from an Italian hospital and improve upon state-of-the-art solvers.

Keywords: OR in health services, Chemotherapy appointment scheduling, multi-objective programming

---

*This paper has been published in European Journal of Operational Research (2025), DOI: `https://doi.org/10.1016/j.ejor.2025.12.023`.

*Corresponding author

1. Introduction

In recent decades, we have seen an increase in cancer incidence in most Western and industrialized countries. According to a study by the International Agency for Research on Cancer on the impact of population aging on the future cancer burden, the global cancer burden is expected to reach more than 35 million cancer cases in 2050, an increase 77% from the 20 million cases estimated in 2022 (Bray et al., 2024). The World Health Organization has identified cancer as the second leading cause of death worldwide, accounting for 10 million deaths in 2020 and one in six deaths worldwide (World Health Organization, 2020). However, there has been a steady decline in the overall rate of cancer death in the past 30 years (Siegel et al., 2024), due to many factors, including advances in prevention, screening, and early detection strategies, the addition of chemotherapy after surgery for some cancers, combined therapies for many cancers, and survival care (Bray et al., 2024).

Characteristics such as the type of cancer, its location, stage, and severity guide the choice of treatment options and their combination. The most widely used traditional treatments are surgery, chemotherapy, and radiation therapy. Modern modalities, including hormonal therapy, anti-angiogenic therapy, stem cell therapy, immunotherapy, and dendritic cell-based immunotherapy, have received increasing attention (Debela et al., 2021). However, chemotherapy remains the most widely used evidence-based treatment for the majority of cancers due to its proven ability to reduce morbidity and mortality (Uttpal et al., 2023).

Recent studies estimate that the number of patients who require first-course chemotherapy per year will increase from 9.8 million to 15.0 million between 2018 and 2040, a relative increase of 53%, and predict a major health crisis driven by unmet demand for chemotherapy (Wilson et al., 2019). This dramatic increase in demand is forcing private and public healthcare organizations to develop improved care delivery solutions. Congestion and workload issues have been reported in many studies, and improved scheduling practices have been identified as a key component to mitigate resource shortages and ensure timely and effective cancer treatment (Issabakhsh et al., 2021; Hesaraki et al., 2020). Poor organization of the outpatient chemotherapy process leads to long waiting times and patient dissatisfaction (Slocum et al., 2021).

To improve resource utilization and patient care, many healthcare organizations have reorganized the delivery of chemotherapy treatments into dedicated facilities, such as outpatient cancer centers or infusion centers (van Harten, 2014; Karakaya et al., 2023). This reorganization process has changed the delivery paradigm from a hospital specialty-based approach to a patient-pathology-based approach, presenting new issues and challenges.

In general, planning and scheduling chemotherapy appointments in outpatient settings involves different levels of hierarchically linked decisions (Lamé et al., 2016; Ahmadi-Javid et al., 2017). At a strategic level, the primary decision concerns the capacity design and dimensioning of the outpatient center in terms of the human and physical resources required for chemotherapy delivery (e.g., nurses, clinicians, pharmacists, paramedical and technical staff, beds, chairs, examination and consultation rooms). At the tactical planning level, the resources available in the cancer center must be allocated to different types of cancer. In particular, the Master Chemotherapy Planning (MCP), that is, the schedule that indicates the days on which the different cancer pathologies are scheduled over a medium-term planning horizon, must be developed, together with the clinician roster that covers the cyclical schedule based on clinician availability, specialization, and skills (Carello et al., 2022; Keshtzari & Norman, 2024).

Then, at an operational level, scheduling patient appointments must be determined on a shorter planning horizon. The latter problem is usually divided into two subproblems (Cataldo et al., 2023): determining the day of the chemotherapy appointment (interday scheduling) and determining the start time of the appointment (intraday scheduling). Generally, on the day of the appointment, patients undergo a blood test first. Then they are visited by a clinician who, depending on the overall clinical conditions, decides whether or not they can receive the chemotherapy treatment. Following the same-day outpatient chemotherapy policy (Hadid et al., 2022b), the steps are carried out on the same day. In contrast, the next-day policy requires the process to take two consecutive days, necessitating that patients who do not live close to the center travel twice in a row.

In this work, we jointly address the interday and intraday scheduling problem at an operational level, assuming a same-day policy. In particular, we address the problem of determining the appointment date and start time for both the oncologist visit and the drug infusion for a set of patients over a one-week planning horizon. The resulting problem belongs to the class of multi-appointment scheduling problems (Marynissen & Demeulemeester, 2020).

The treatment plans are determined by oncologists according to existing chemotherapy protocols, informed by clinical trials. Chemotherapy is given in cycles with rest periods during and between each cycle. The number and duration of cycles vary depending on the type of cancer and the stage of the disease, and patients must follow their treatment plan to achieve the best health outcomes. We schedule appointments over a week, assuming that all the patients who must be treated in that week are known, based on the treatment plan. A week is a sufficiently short planning period to ensure that treatment is both timely and effective, regardless of the day of the week on which the patient receives it. As the MCP generally assigns more than one day per week to each pathology, the day on which a patient receives the infusion must also be decided.

We consider several criteria and metrics that represent both the perspectives of cancer center management and patients. Specifically, we formulate the problem as a multi-objective optimization problem aimed at minimizing the overtime required to reach the regular opening time of the center, minimizing the patient waiting time on the appointment day, and maximizing the patient preferences for beds or chairs to receive the infusion. Indeed, due to the large number of requests and limited resources available, some overtime may be required to meet all requests. However, overtime has an impact on the workload and the quality of work for clinicians and nurses. For this reason, we optimize the inter-day and intra-day schedules to reduce overtime as much as possible. Waiting time is a crucial quality indicator that impacts patient satisfaction, and its reduction enhances the patient's treatment experience, ultimately improving patient care and outcomes (Rezaeiahari & Khasawneh, 2017). Finally, focusing on a patient-centered perspective, the last metric takes into account patient preferences regarding the place where they receive the drug infusion (chair or bed). Critical patients require infusion in bed due to their clinical status, whereas non-critical patients prefer to receive chemotherapy infusion in a chair, allowing them to read a book or chat with other patients.

Since the objectives are not equally important, we model the problem using a lexicographic approach and solve it by optimizing a sequence of Mixed Integer Linear Programming (MILP) models. When problems turn out to be computationally challenging, we propose bounds and warm starts based on decomposition heuristics to accelerate the solution process.

The paper is organized as follows. In Section 2, the relevant literature on patient appointment planning and scheduling for chemotherapy treatments is analyzed. The problem and the multi-objective formulation are described in Section 3. The proposed solution approaches for each problem are reported and explained in Section 4, whereas the results are discussed in Section 5. Finally, conclusions and further developments are given in Section 6.

2. Literature review and contribution of the paper

Chemotherapy planning and scheduling encompass numerous problems and challenges in various areas, including determining optimal drug combinations, dosages, and treatment cycles, planning treatments, scheduling patient appointments, and allocating the primary resources involved in the care process (Saville et al., 2019). In the past, researchers' attention has been mainly focused on the medical aspects of the problem. Many papers have been published proposing methods dealing with dosing and treatment duration of cancer chemotherapy plans, balancing the benefits of treating tumors with the adverse toxic side effects caused by the anti-cancer drugs and taking into account several factors, such as tumor growth features and drug infusion rates (Agur et al., 2006; Shi et al., 2014; Sbeity & Younes, 2015; Abdulrashid et al., 2024).

More recently, the scientific literature has also focused on operations management and organizational issues related to the chemotherapy delivery process.

In Lamé et al. (2016), the first systematic literature review on outpatient chemotherapy planning is reported. The review categorizes the papers based on several key features, including the planning level (strategic, tactical, and operational), the study's objective and related performance metrics, the types and quantities of resources, and the sources of uncertainty considered. An updated, optimization-oriented systematic literature review of papers published between 2009 and 2021 is reported in Hadid et al. (2022a). The authors first classified the contributions into three groups depending on the main problem addressed, i.e., planning, scheduling, and assignment problems. Then, the 45 publications selected have been classified with respect to the scope of the analysis, the considered complexities, the modeling techniques, and the proposed solution methods. A recent review by Bazrafshan & Lam (2025) provides a comprehensive and up-to-date overview of research on outpatient chemotherapy planning and decision-making. The review encompasses 99 studies, which are categorized based on decision level, problem scope, performance metrics and objectives, complexity factors, methodological approach, and solution techniques.

In line with the above-referenced classifications, we focus the analysis of the literature on studies published in international journals between 2019 and 2024 that deal with chemotherapy appointment planning and scheduling problems at an operational level of decision, also referred to as interday and intraday appointment scheduling (Cataldo et al., 2023).

The problem of determining the appointment date of a set of patients to be treated within a specific time horizon (interday scheduling) has been tackled by proposing exact formulations, heuristics, and meta-heuristics (Hadid et al., 2022a). Some papers jointly considered patient-to-resource assignment decisions, such as those involving nurses, oncologists, beds, chairs, and pharmacists. Hesaraki et al. (2020) proposed a multi-criteria MILP model based on a three-stage heuristic to minimize the number of deferring times for scheduled appointments, taking into account nurse capacity constraints. In Wenzel et al. (2024), the authors focus on the interday problem of assigning chemotherapy sessions in a network of treatment centers to identify effective multi-appointment scheduling policies that exploit the total capacity of a networked system. The problem is modeled as a Markov decision process, which is then solved approximately using techniques of approximate dynamic programming.

The intraday chemotherapy outpatient scheduling problem has been tackled in Hesaraki et al. (2019), where the authors developed an ILP model to assign the appointment slots to patients subject to nursing constraints. They use a parametric multi-objective function to minimize both the weighted flowtime and the makespan. In Lyon et al. (2022), an ILP model is proposed to schedule all patients assigned to a short planning horizon, accounting for the preparation time required for administering the drug. To solve the problem, they proposed a linear relaxation of the model, based on treatment patterns, solved via column generation. The same-day chemotherapy outpatient scheduling problem has been tackled in Corsini et al. (2022) as a multi-stage problem to reduce idle times within and among the medical consultation, drug preparation, and infusion. Agnetis et al. (2019) modeled the multi-stage appointment problem as a deterministic flexible job shop in which patients correspond to jobs and activities to the stages of the patient flow within the cancer clinic. The objective of the model is to minimize the total time spent by patients on the day of treatment.

Many papers approached the daily scheduling problem introducing some sources of uncertainty. In Issabakhsh et al. (2021), a MILP robust slack allocation model is designed to find the optimal patient appointment schedule, considering infusion duration longer than expected. The model minimizes the weighted sum of the total waiting times of patients, the makespan, and the number of beds used through the planning horizon. A robust scheduling heuristic is developed based on the adaptive large neighborhood search to determine patient appointments of real-size infusion centers. Han et al. (2024) tackle the problem of scheduling chemotherapy visits with multiple appointments requiring different resources. The study utilizes artificial neural networks to calculate patient no-show probabilities and appointment durations, which are subsequently incorporated into the optimization models. The problem of sequencing patients for a one-day session of chemotherapy infusion, which considers the uncertainty related to the patient's inability to receive the treatment, is solved in Garaix et al. (2020) using a stochastic optimization model. The same problem has been addressed in Hooshangi-Tabrizi et al. (2020), which proposes an online optimization approach based on an adaptive and flexible procedure that combines two optimization models. The first model schedules incoming appointment requests, while the second one reschedules already booked appointments with the goal of better allocating resources, on a daily basis, as new information becomes available. A slightly different version of the problem is considered in Karakaya et al. (2023), where the scheduling of patient appointments and the assignment of patients to nurses on a given day are addressed, taking into account the uncertainty in infusion durations. To solve the problem, the authors formulated a two-stage stochastic MILP model to minimize the expected weighted sum of excess patient acuity, waiting time, and nurse overtime. The problem of daily patient scheduling and assignment to nurses and chairs, in the presence of uncertainty in infusion durations, has also been studied by Gul (2024). The authors developed a two-stage stochastic mixed integer programming model to minimize the expected weighted cost of patient waiting time and nurse overtime, and proposed a grouping-based decomposition algorithm to solve the model. Similarly, in Celik et al. (2025), the authors adopt a risk/inequity-averse perspective, introducing a metric that penalizes excess waiting and inequity among patient waiting times. To solve the problem, they developed an exact solution method based on scenario reduction algorithms, integrated within a binary search framework. Finally, the approach presented in Ozyuksel et al. (2025) addresses the daily scheduling problem by integrating oncologist consultation and chemotherapy scheduling. The authors develop a two-stage stochastic MIP model to consider the uncertainty of the infusion durations and the possible chemotherapy treatment approvals after consultations.

Few papers consider both interday and intraday decisions. The approaches proposed in these studies can be categorized into two classes: integrated approaches, where decisions are considered simultaneously, and sequential ones that solve the considered problems sequentially and separately (Ahmadi-Javid et al., 2017). In Heshmat & Eltawil (2021), a two-phase sequential approach is proposed. First, a MILP model determines the day of treatment for a set of patients and identifies the optimal number of nurses and pharmacists required. Then, in the second phase, a discrete-event simulation model is used to generate patient appointment schedules that minimize treatment delays for patients and the total completion times of treatments each day. Similarly, in Benzaid et al. (2020), a two-stage procedure for scheduling chemotherapy appointments for new patients and assigning the daily patient mix to available nurses is introduced. In the first phase, new patient appointments are assigned at the end of each day, and the daily nurse requirement is determined. In the second phase, patients are assigned to nurses, minimizing the number of nurses required. In Cataldo et al. (2023), a two-phase solution approach is developed to address interday and intraday scheduling, determining the date and time slot for infusions of a set of patients to be scheduled. The two subproblems have been solved sequentially with optimization models developed for each phase. The solutions have been evaluated in terms of makespan, resource utilization, overtime, and patient diversion metrics. The work proposed by Hesaraki et al. (2023) simultaneously addresses the interday and intraday scheduling problems, using a fixed template of slots for the online scheduling of appointments, with a focus on drug administration.

To the best of our knowledge, there are no papers in the literature that deal with the integrated interday and intraday problem in a multi-appointment setting. Only three papers (Corsini et al., 2022; Han et al., 2024; Ozyuksel et al., 2025) address the same-day scheduling problem, considering more than one activity to be executed in sequence within a given planning horizon. However, they do not simultaneously tackle the problem of determining both the date and time of the appointments.

As for the objective functions considered in the studies, time and cost metrics received more attention than workload and satisfaction measures (Hadid et al., 2022a). Only one paper seeks to maximize patient preferences (Hooshangi-Tabrizi et al., 2020).

The novelty of this paper is twofold. First, we jointly address the integrated interday and intraday multi-appointment scheduling considering patients-to-multiple-resources assignment. To the best of our knowledge, this is the first attempt to integrate patient-centered operational decisions in a unified approach that follows the trajectory of patients in the cancer center throughout the day of treatment. The integrated planning and scheduling solution determines simultaneously, for a short-term planning horizon (usually a week), the day of the appointment (planning decision) as well as the starting time of the oncologist visit and the infusion (scheduling decision) for a set of patients to be scheduled according to the treatment plans. The clinical consistency of the treatment plans is ensured as the set of patients to be treated each week has been determined based on the treatment plans and cycles. The assignment of patients to the available beds and chairs is also determined. Secondly, following a patient-centered approach, we combine different metrics proposed in previous studies, such as minimizing overtime, minimizing patient waiting time, and maximizing patient preferences, into a multi-objective optimization approach, where the ultimate aim is to minimize patient discomfort.

3. Problem description and formulation

3.1. Problem description

We consider a multi-appointment framework, in which each patient must complete two steps on the same day: first, the clinician's consultation (visit) and then the chemotherapy treatment (infusion). We address the problem of determining both the appointment date for a set P of patients and the start times of the consultation visit and chemotherapy infusion.

For each patient p, the visit duration v_p and the infusion duration f_p are given, and assumed to be deterministic values. Patients are classified into a set K of cancer pathologies: the binary parameter u_{pk} equals 1 if the main pathology of patient p is k, and 0 otherwise.

We consider a planning horizon represented by a set D of days, typically one working week in length. Although some treatment plans may require more than one infusion per week, in our setting, infusions are scheduled every two or three weeks. Therefore, we assume that each patient requires one appointment within the considered one-week horizon and that all patients must be scheduled. Patients are included in the weekly scheduling horizon only if their treatment is due according to their clinical regimen. Thus, the model optimizes appointment day and time within the operational 5-day horizon, preserving the medical effectiveness of the prescribed treatment cycles.

Each working day $d \in D$ is divided into a set S^I of time slots. The set S^I also contains a given number of overtime slots. The last time slot available for infusions in the regular opening time of the center is denoted as N^I, where $N^I < |S^I|$. The subset of time slots devoted to visits remains the same every working day and is denoted as $S^V \subseteq S^I$. As for the infusions, S^V also includes overtime slots, while the regular time for visits is limited to N^V, where $N^V < |S^V|$.

Consultations take place in examination rooms. The set of consulting rooms is denoted as R. We assume that each consulting room is dedicated to a single pathology on each day: let the binary parameter w_{rkd} be equal to 1 if room r is dedicated to pathology k on day d, otherwise equal to 0, according to an MCP obtained as a result of the tactical level decision. For the infusion, we can use either chairs or beds, depending on the patient's clinical condition. The sets of beds and chairs are denoted with B and C, respectively.

The set P of patients is partitioned into two subsets: P_B contains the patients who must receive the infusion in a bed (*critical patients*), while the patients in $P \setminus P_B$ can receive the infusion either in a chair or in a bed (*non-critical patients*). Note that, based on patient preference, we assume that non-critical patients prefer to receive the infusions in a chair.

We made the following assumptions regarding the system setting and the related problem addressed:

- The laboratory for the blood tests and the pharmacy for the drug preparation are located in the outpatient center and are always able to meet the demand and match the start times of the scheduled infusion appointments (see Hesaraki et al. (2019); Heshmat et al. (2018) for similar assumptions);

- Nursing staff members are exclusively dedicated to the oncology outpatient center, do not share duties with other departments, and operate under a functional care delivery model, as discussed by Liang & Turkan (2016);

- Nursing capacity is strategically scaled in proportion to available beds and infusion chairs, ensuring that nurses can efficiently manage scheduled patient flows without critical time misalignment or inefficiencies. This modeling approach is consistent with established literature (Ahmadi-Javid et al., 2017; Hesaraki et al., 2023);

- Our problem focuses explicitly on the optimal allocation of patients to examination rooms, infusion chairs, and beds, which are the resources identified as most critical for operational efficiency in the considered clinical environment (see Garaix et al. (2020); Mandelbaum et al. (2020); Slocum et al. (2021); Lyon et al. (2022); Ozyuksel et al. (2025) for similar assumptions);

- The allocation of the available cancer center visit capacity to the various cancer types is a priori determined, at a tactical level, in order to satisfy the demand of patients and guarantee the clinician's coverage of the schedule (Carello et al., 2022; Keshtzari & Norman, 2024).

To treat all patients, overtime may be necessary, either for visits, infusions, or both. However, from a management and nursing perspective, overtime should be avoided whenever possible. Therefore, we first address the problem of minimizing overtime. However, minimizing overtime is not the only goal. From a patient's point of view, we also want to minimize the time they spend in the center on the day of their appointment. Finally, to minimize patient discomfort, we want to assign as many non-critical patients as possible to chairs. The three objectives are not equally relevant, so the problem is treated as a multi-objective problem with a lexicographic objective function.

The problem belongs to the family of multi-appointment scheduling problems (Marynissen & Demeulemeester, 2020), which jointly address the integrated interday (appointment day) and intraday (appointment time) scheduling, as well as the patient allocation to multiple resources problem (Ahmadi-Javid et al., 2017). It shares features with the flexible flow shop problem (or hybrid flow shop), where all jobs must be processed on the same set of different stages (Pinedo, 2022). Parallel machines are available at each stage. In the problem considered, patients act as jobs that must go through two stages: examination rooms act as first-stage machines, while chairs and beds act as second-stage machines. However, it is more complex than the flexible

Sets	
P	set of patients
P_B	set of critical patients
K	set of pathologies
D	set of days in the planning horizon
S^I	set of time slots available for infusions in one day
S^V	set of time slots available for visits in one day
R	set of examination rooms
B	set of beds
C	set of chairs
Parameters	
$u_{pk} \in \{0,1\}$	1 if the main pathology of patient $p \in P$ is $k \in K$, 0 otherwise
$w_{rkd} \in \{0,1\}$	1 if room r is assigned to pathology $k \in K$ in day $d \in D$, 0 otherwise
v_p	consultation visit duration of patient $p \in P$
f_p	infusion duration of patient $p \in P$
N^V	last time slot available for visits (regular time)
N^I	last time slot available for infusions (regular time)

Table 1: Sets and parameters.

flow shop problem, as not all machines can process every job. In fact, patients are partitioned into subsets. For the first stage (visit), patients are partitioned based on their pathology, and a patient can be treated only in the rooms selected for their pathology. For the second stage (infusion), patients are partitioned into critical and non-critical groups based on their clinical condition, regardless of their underlying pathology. They cannot be treated by an arbitrary machine: critical patients must be assigned to beds only. It is worth noting that patients belonging to different subsets in the first stage, namely those with different pathologies, may share resources and machines in the second stage, and vice versa.

The problem can be proved to be NP-hard. In fact, consider the problem where patients can only receive infusions on chairs, and minimizing overtime is the objective function. Then, the bin packing problem can be reduced to the latter problem, where patients are the items and chairs are the bins. Thus, even such a special case of the problem is NP-hard.

The problem formulation is described in the following sections. The notation used is summarized in Table 1.

3.2. Formulation: main variables and constraints

The formulation utilizes two sets of variables: a set of main variables, which include the day and start time of the visit and infusion for each patient, and a set of auxiliary variables used to formulate the objective functions.

The first family of main variables gives, for each patient p, the day and starting time of the visit, which can be any time slot $s \in S^V$, since we assume that visits (and infusions) can start in overtime:

$$x_{pds} = \begin{cases} 1 & \text{if patient } p \in P \text{ starts the visit in day } d \in D \text{ at time slot } s \in S^V, \\ 0 & \text{otherwise.} \end{cases}$$

The second family of main variables assigns to each critical patient $p \in P_B$ a start time for the infusion in the set S^I:

$$y_{pds} = \begin{cases} 1 & \text{if patient } p \in P_B \text{ starts the infusion (in a bed) in day } d \in D \text{ at time slot } s \in S^I, \\ 0 & \text{otherwise.} \end{cases}$$

For non-critical patients, two additional families of main variables are introduced to determine whether the patient is receiving the infusion in a bed or a chair, and when the infusion starts:

$$z^B_{pds} = \begin{cases} 1 & \text{if patient } p \in P \setminus P_B \text{ starts the infusion in a bed in day } d \in D \text{ at time slot } s \in S^I, \\ 0 & \text{otherwise,} \end{cases}$$

and

$$z^C_{pds} = \begin{cases} 1 & \text{if patient } p \in P \setminus P_B \text{ starts the infusion in a chair in day } d \in D \text{ at time slot } s \in S^I, \\ 0 & \text{otherwise.} \end{cases}$$

The main variables are subject to the following constraints:

$$\sum_{d \in D} \sum_{s \in S^V} x_{pds} = 1 \qquad \forall p \in P, \tag{1}$$

$$\sum_{\substack{p \in P: \\ u_{pk}=1}} \sum_{q=\max\{1,\ s+1-v_p\}}^{s} x_{pdq} \le \sum_{r \in R} w_{rkd} \qquad \forall d \in D, s \in S^V, k \in K, \tag{2}$$

$$\sum_{s \in S^V} x_{pds} = \sum_{s \in S^I} y_{pds} \qquad \forall d \in D, p \in P_B, \tag{3}$$

$$\sum_{s \in S^V} x_{pds} = \sum_{s \in S^I} \left(z^B_{pds} + z^C_{pds} \right) \qquad \forall d \in D, p \in P \setminus P_B, \tag{4}$$

$$\sum_{s \in S^V} (s + v_p) x_{pds} \le \sum_{s \in S^I} s\, y_{pds} \qquad \forall d \in D, p \in P_B, \tag{5}$$

$$\sum_{s \in S^V} (s + v_p) x_{pds} \le \sum_{s \in S^I} s \left(z^B_{pds} + z^C_{pds} \right) \qquad \forall d \in D, p \in P \setminus P_B, \tag{6}$$

$$\sum_{p \in P \setminus P_B} \sum_{q=\max\{1,\ s+1-f_p\}}^{s} z^C_{pdq} \le |C| \qquad \forall d \in D, s \in S^I, \tag{7}$$

$$\sum_{p \in P_B} \sum_{q=\max\{1,\ s+1-f_p\}}^{s} y_{pdq} + \sum_{p \in P \setminus P_B} \sum_{q=\max\{1,\ s+1-f_p\}}^{s} z^B_{pdq} \le |B| \qquad \forall d \in D, s \in S^I. \tag{8}$$

Constraints (1) guarantee that each patient is visited exactly once in the planning horizon. Constraints (2) guarantee that the number of patients visited in time slot s of day d is not greater than the number of examination rooms assigned to the patient's main pathology on day d. We recall that the main pathology of p is described by the parameter u_{pk} and the number of rooms assigned to pathology k on day d is given by $\sum_{r \in R} w_{rkd}$. Constraints (3)–(4) guarantee, for critical and non-critical patients, respectively, that the visit and the infusion must take place on the same day. Notice that constraints (4), together with constraints (1), ensure that the right-hand side of (4) is less than or equal to 1, that is, any non-critical patient does not get both a chair and a bed. Constraints (5)–(6) guarantee, for critical and non-critical patients, respectively, that the infusion will start only after the end of the consultation visit. Constraints (7)–(8) guarantee that, for each day, the number of patients receiving the infusion in each time slot is not greater than the number of available chairs $|C|$ or beds $|B|$, respectively.

3.3. Formulation: goals and auxiliary variables

The first goal is to minimize the total overtime. To this end, we introduce two auxiliary variables: $\alpha_d^V \in \mathbb{R}_+$ and $\alpha_d^I \in \mathbb{R}_+$, which represent the maximum overtime on day d related to visits and infusions, respectively. They are defined as the difference between the end of the last visit (or infusion) and the last slot in regular time. The overtime variables are linked to the main variables as follows:

$$\alpha_d^V \geq \sum_{s \in S^V} (s + v_p - 1) x_{pds} - N^V \qquad \forall d \in D,\ p \in P, \tag{9a}$$

$$\alpha_d^I \geq \sum_{s \in S^I} (s + f_p - 1) y_{pds} - N^I \qquad \forall d \in D,\ p \in P_B, \tag{9b}$$

$$\alpha_d^I \geq \sum_{s \in S^I} (s + f_p - 1)(z_{pds}^B + z_{pds}^C) - N^I \qquad \forall d \in D,\ p \in P \setminus P_B. \tag{9c}$$

Constraints (9a) force the value of the variable α_d^V on day d to be greater than or equal to the difference between the last slot of the visit of each patient and the last available time slot for the visit in regular time N^V. It forces a positive overtime only if at least one patient finishes the visit in overtime. Similarly, constraints (9b)–(9c) set the value of the variable α_d^I for infusions on day d, considering critical and non-critical patients, respectively. Thus, the first metric (to be minimized) is formulated as follows:

$$F_1(\alpha^V, \alpha^I) := \sum_{d \in D} (\alpha_d^V + \alpha_d^I).$$

Minimizing F_1 guarantees that if at least one patient finishes the visit or the infusion in overtime, the largest overtime values are taken.

The second goal is to minimize the time that patients spend in the center. Since the visit and infusion durations are given for each patient, the second objective results in minimizing the waiting time of the patients, namely the difference between the start of the infusion and

Variables	
$x_{pds} \in \{0,1\}$	1 if patient $p \in P$ starts the visit in day $d \in D$ at time slot $s \in S^V$, 0 otherwise
$y_{pds} \in \{0,1\}$	1 if patient $p \in P_B$ starts the infusion (in a bed) in day $d \in D$ at time slot $s \in S^I$, 0 otherwise
$z^B_{pds} \in \{0,1\}$	1 if patient $p \in P \setminus P_B$ starts the infusion in a bed in day d at time slot $s \in S^I$, 0 otherwise
$z^C_{pds} \in \{0,1\}$	1 if patient $p \in P \setminus P_B$ starts the infusion in a chair in day d at time slot $s \in S^I$, 0 otherwise
$\alpha^V_d \in \mathbb{R}_+$	maximum overtime for visits on day $d \in D$
$\alpha^I_d \in \mathbb{R}_+$	maximum overtime for infusions on day $d \in D$
$\omega_d \in \mathbb{R}_+$	maximum waiting time among patients in day $d \in D$
Objective functions	
$F_1(\alpha^V, \alpha^I)$	$= \sum_{d \in D} (\alpha^V_d + \alpha^I_d)$, sum of the maximum overtime for visits and infusions in each day
$F_2(\omega)$	$= \sum_{d \in D} \omega_d$, sum of the maximum waiting times in each day
$F_3(z^C)$	$= \sum_{p \in P \setminus P_B} \sum_{d \in D} \sum_{s \in S^I} z^C_{pds}$, number of non-critical patients who receive the infusion in a chair

Table 2: Variables and objective functions.

the end of the visit. To obtain a balanced metric for this goal, we decided to minimize the sum of the maximum waiting times among patients on each day. We define the auxiliary variable $\omega_d \in \mathbb{R}_+$ which represents the maximum waiting time on day d for all patients. This auxiliary variable is linked to the main variables as follows:

$$\omega_d \geq \sum_{s \in S^I} s y_{pds} - \sum_{s \in S^V} (s + v_p) x_{pds} \qquad \forall d \in D,\ p \in P_B, \tag{10a}$$

$$\omega_d \geq \sum_{s \in S^I} s (z^B_{pds} + z^C_{pds}) - \sum_{s \in S^V} (s + v_p) x_{pds} \qquad \forall d \in D,\ p \in P \setminus P_B. \tag{10b}$$

Hence, the second metric (to be minimized) can be formulated as follows:

$$F_2(\omega) := \sum_{d \in D} \omega_d.$$

Finally, we want to consider the preferences of non-critical patients. Although they can receive the infusion in a bed or a chair, the chair is the most comfortable and preferred choice. The corresponding metric (to be maximized) takes into account the preferences met and can be represented as follows:

$$F_3(z^C) := \sum_{p \in P \setminus P_B} \sum_{d \in D} \sum_{s \in S^I} z^C_{pds}.$$

As mentioned, the three objectives are not equally important: minimizing F_1 is more important than minimizing F_2, which, in turn, is more important than maximizing F_3.

Table 2 summarizes the variables and objectives used in our approach.

4. Solution approach

We tackle the lexicographic multi-objective problem by solving a sequence of three problems and applying an ϵ-constrained approach. When we optimize an objective, we force the value of the previously optimized objectives to their best value.

The first problem aims to minimize the total overtime of visits and infusions and is modeled as follows:

$$\begin{cases} \min\limits_{(x,y,z^B,z^C,\alpha^V,\alpha^I)} & F_1(\alpha^V,\alpha^I) \\ \text{subject to} & (1)-(9). \end{cases} \tag{$\mathcal{P}_1$}$$

The optimal value of $(\mathcal{P}_1)$ is stored in the parameter $\bar{v}_1$.

We then consider the second problem, which aims to find, among all the equivalent optimal solutions of $(\mathcal{P}_1)$, one that minimizes the sum of the daily maximum waiting times. The problem $(\mathcal{P}_2)$ is formulated as follows:

$$\begin{cases} \min\limits_{(x,y,z^B,z^C,\alpha^V,\alpha^I,\omega)} & F_2(\omega) \\ \text{subject to} & (1)-(10) \\ & F_1(\alpha^V,\alpha^I) \le \bar{v}_1. \end{cases} \tag{$\mathcal{P}_2$}$$

The optimal value of $(\mathcal{P}_2)$ is stored in the parameter $\bar{v}_2$.

Finally, the third problem aims to maximize the number of non-critical patients receiving infusion on a chair, while keeping the total overtime and the sum of the daily maximum waiting times not worse than $\bar{v}_1$ and $\bar{v}_2$, respectively. The resulting formulation of the problem $(\mathcal{P}_3)$ follows:

$$\begin{cases} \max\limits_{(x,y,z^B,z^C,\alpha^V,\alpha^I,\omega)} & F_3(z^C) \\ \text{subject to} & (1)-(10) \\ & F_1(\alpha^V,\alpha^I) \le \bar{v}_1 \\ & F_2(\omega) \le \bar{v}_2. \end{cases} \tag{$\mathcal{P}_3$}$$

To speed up the solution process, we enriched the formulation of $(\mathcal{P}_1)$ with a bound on the objective function value and applied decomposition-based heuristics as a warm start for $(\mathcal{P}_2)$ and $(\mathcal{P}_3)$.

4.1. Solving problem $(\mathcal{P}_1)$

To solve $(\mathcal{P}_1)$ efficiently, we enforce the formulation with an additional valid inequality that sets a lower bound LB_1 on the objective function. We then solve the enriched formulation:

$$\begin{cases} \min\limits_{(x,y,z^B,z^C,\alpha^V,\alpha^I)} & F_1(\alpha^V,\alpha^I) \\ \text{subject to} & (1)-(9) \\ & F_1(\alpha^V,\alpha^I) \ge LB_1. \end{cases}$$

Procedure 1: Computing the value of lower bound LB_1

/* Find the set of pathologies with an insufficient number of time slots for visits */

1 $\overline{K} \leftarrow \emptyset$

2 **for** $k \in K$ **do**

3 $\quad AvailableSlots \leftarrow N^V \left(\sum_{r \in R} \sum_{d \in D} w_{rkd} \right)$

4 $\quad NeededSlots \leftarrow \sum_{\substack{p \in P: \\ u_{pk}=1}} v_p$

5 $\quad$ **if** $AvailableSlots < NeededSlots$ **then**

6 $\quad\quad \overline{K} \leftarrow \overline{K} \cup \{k\}$

7 $\quad$ **end**

8 **end**

9 $\overline{P} \leftarrow \bigcup_{k \in \overline{K}} \{p \in P : \ u_{pk} = 1\}$

/* Solve the continuous relaxation $(\mathcal{P}_1^r)$ of $(\mathcal{P}_1)$, where only patients in the set $\overline{P}$ are considered and the number of chairs and beds is supposed to be unlimited */

10 Find an optimal solution for the problem:

$$\begin{cases} \min\limits_{(x,y,z^B,z^C,\alpha^V,\alpha^I)} & F_1(\alpha^V, \alpha^I) \\ \text{subject to} & (1)-(6),\ (9) \\ & x, y, z^B, z^C \in [0,1] \end{cases} \qquad (\mathcal{P}_1^r)$$

where the variables x_{pds}, y_{pds}, z^B_{pds}, z^C_{pds} are restricted to $p \in \overline{P}$

11 $LB_1 \leftarrow$ optimal value of $(\mathcal{P}_1^r)$

The procedure for calculating LB_1 is described in Procedure 1. First, we identify the set $\overline{K}$ of pathologies that have an insufficient number of time slots for visits according to the given MCP. The set $\overline{K}$ is given by pathologies k such that the number of time slots available for visits, equal to $N^V \left(\sum_{r \in R} \sum_{d \in D} w_{rkd} \right)$, is less than the number of time slots needed for visits, i.e., $\sum_{\substack{p \in P: \\ u_{pk}=1}} v_p$, (lines 1-8). We denote by $\overline{P}$ the set of patients whose main pathology belongs to $\overline{K}$ (line 9). The set $\overline{P}$ provides a subset of patients who generate overtime in terms of visits and, possibly, infusions. We then solve $(\mathcal{P}_1^r)$, i.e., the continuous relaxation of $(\mathcal{P}_1)$, considering only patients in $\overline{P}$ and assuming an unlimited number of beds and chairs (lines 10-11). The optimal value LB_1 of $(\mathcal{P}_1^r)$ is a lower bound on the total overtime, hence

$$F_1(\alpha^V, \alpha^I) \geq LB_1 \tag{11}$$

is a valid inequality for $(\mathcal{P}_1)$. In Section 5.2 we will show the impact of adding (11) to $(\mathcal{P}_1)$.

4.2. Solving problem $(\mathcal{P}_2)$

Problem $(\mathcal{P}_2)$ proves to be more computationally challenging than $(\mathcal{P}_1)$; thus, we compute a heuristic solution which is used as a warm start (Procedure 2).

Procedure 2: Finding an optimal solution of $(\mathcal{P}_2)$

1 Find an optimal solution $(\bar{x}, \bar{y}, \bar{z}^B, \bar{z}^C, \bar{\alpha}^V, \bar{\alpha}^I)$ of $(\mathcal{P}_1)$

`/* Fix the set of patients treated each day */`

2 **for** $d \in D$ **do**

3 $\quad P_d \leftarrow \left\{ p \in P : \sum_{s \in S^V} \bar{x}_{pds} = 1 \right\}$

4 **end**

`/* Once the set of patients treated each day is fixed, solve problem` $(\mathcal{P}_2)$ `by decomposing it into a set of problems one for each day */`

5 **for** $\delta \in D$ **do**

6 $\quad$ find an optimal solution of $(\mathcal{P}_2)$ restricted to the day δ:

$$\begin{cases} \min\limits_{(x,y,z^B,z^C,\alpha^V,\alpha^I,\omega)} & \omega_\delta \\ \text{subject to} & (1) - (10) \\ & \alpha^V_\delta = \bar{\alpha}^V_\delta \\ & \alpha^I_\delta = \bar{\alpha}^I_\delta \end{cases}$$

$\quad$ where the variables x_{pds}, y_{pds}, z^B_{pds}, z^C_{pds}, α^V_d, α^I_d and ω_d are restricted to $p \in P_\delta$, and $d = \delta$

7 **end**

`/* Solve` $(\mathcal{P}_2)$ `with warm start */`

8 Use the union of the solutions found at lines 5–7 as a warm start to solve the whole problem $(\mathcal{P}_2)$

First, we solve the problem $(\mathcal{P}_1)$ (line 1) and fix the set P_d of patients treated each day d (lines 2-4). Then, we solve the problem $(\mathcal{P}_2)$, where the day of treatment of each scheduled patient is fixed. This last problem can be decomposed into a set of $|D|$ problems, where each problem considers a single day δ and the corresponding set of patients P_δ. The start time of visits and infusions is optimized, while the overtime variables α^V_δ and α^I_δ are set equal to the value obtained by solving $(\mathcal{P}_1)$. The maximum waiting time of patients ω_δ is minimized (lines 5-7), solving $(\mathcal{P}_2)$ restricted to day δ. Finally, the union of the single-day solutions is used as a warm start to solve the whole problem $(\mathcal{P}_2)$ (line 8). In the last step, we impose that the total overtime for visits and infusions is optimal, i.e., $F_1(\alpha^V, \alpha^I) \leq \bar{v}_1$, and we solve $(\mathcal{P}_2)$. However, we allow visit and infusion days and start times to be different from those obtained in the optimal solution of $(\mathcal{P}_1)$.

4.3. Solving problem $(\mathcal{P}_3)$

The problem $(\mathcal{P}_3)$ turns out to be more computationally demanding than $(\mathcal{P}_1)$ and $(\mathcal{P}_2)$. As for $(\mathcal{P}_2)$, we use a warm start solution computed by decomposing the problem. First, we add a step aimed at achieving a balanced decomposition: we search for a feasible solution of $(\mathcal{P}_3)$ in which the total infusion duration of non-critical patients is as balanced as possible over the days of the planning horizon $(\mathcal{P}^b_3)$. The problem $(\mathcal{P}^b_3)$ uses the auxiliary variables $\beta_{dt} \in \mathbb{R}_+$, which are the absolute value of the difference between the total infusion duration of non-critical patients on day d and t, where $d < t$. The problem $(\mathcal{P}^b_3)$ is formulated as follows, where the additional constraints enforce the values of the variables β_{dt}:

$$\left\{\begin{array}{lll} \min & \sum_{d \in D} \sum_{\substack{t \in D:\\ t>d}} \beta_{dt} & \\ \text{subject to} & \beta_{dt} \geq \left[\sum_{p \in P \setminus P_B} \sum_{s \in S^V} f_p\, x_{pts}\right] - \left[\sum_{p \in P \setminus P_B} \sum_{s \in S^V} f_p\, x_{pds}\right] & \forall\ d, t \in D:\ d < t, \\ & \beta_{dt} \geq \left[\sum_{p \in P \setminus P_B} \sum_{s \in S^V} f_p\, x_{pds}\right] - \left[\sum_{p \in P \setminus P_B} \sum_{s \in S^V} f_p\, x_{pts}\right] & \forall\ d, t \in D:\ d < t, \\ & (1) - (10), & \\ & F_1(\alpha^V, \alpha^I) \leq \bar{v}_1, & \\ & F_2(\omega) \leq \bar{v}_2. & \end{array}\right. \qquad (\mathcal{P}_3^b)$$

The overall approach used to solve $(\mathcal{P}_3)$ is described in Procedure 3. First, we apply Procedure 2 to find the optimal values $\bar{v}_1$ and $\bar{v}_2$ of $(\mathcal{P}_1)$ and $(\mathcal{P}_2)$, respectively (line 1). Then, we find an optimal solution of $(\mathcal{P}_3^b)$. Given the optimal solution of problem $(\mathcal{P}_3^b)$, we fix the set of patients to be treated on each day (lines 3-5) and we solve problem $(\mathcal{P}_3)$. This last problem is decomposed into a set of $|D|$ problems, where each problem considers a single day δ and the corresponding set of patients P_δ. The start time of visits and infusions is optimized, while the overtime variables α_δ^V, α_δ^I, and ω_δ are set equal to the value obtained by solving $(\mathcal{P}_3^b)$. The number of non-critical patients receiving the infusion in a chair is maximized (lines 6-8). Finally, the union of the single-day solutions is used as a warm start for solving problem $(\mathcal{P}_3)$ (line 9).

5. Computational results

The formulations and approaches described in Sections 3 and 4 have been implemented in AMPL. The MILP models were solved using Gurobi 11.0.0. The tests were performed on an Apple M1 MAX equipped with a 64 GB RAM, running under MacOS 13.4.

We compare the results of our approaches with those obtained by Gurobi on the formulations. Different time limits have been set for the different steps of the approaches:

- the time limit for solving the problems $(\mathcal{P}_1^r)$ and $(\mathcal{P}_1)$ is 300 seconds each;
- the time limit for solving $(\mathcal{P}_2)$ with the solver is 3600 seconds; as for Procedure 2, the time limit for solving each one-day problem is 120 seconds (hence the overall decomposition heuristic is given 600 seconds); the solution of $(\mathcal{P}_2)$ with warm start is given 3000 seconds to make the comparison fair;
- 7200 seconds have been allocated to solve $(\mathcal{P}_3)$ with the solver; 120 seconds have been allocated to $(\mathcal{P}_3^b)$ and each one-day problem (hence the time limit for the decomposition heuristic is 600 seconds), and 6600 seconds have been allocated to the solver to solve $(\mathcal{P}_3)$ with warm start.

Procedure 3: Finding an optimal solution of $(\mathcal{P}_3)$

1 Apply Procedure 2 to find the optimal values $\bar{v}_1$ and $\bar{v}_2$ of $(\mathcal{P}_1)$ and $(\mathcal{P}_2)$, respectively

/* Find a feasible solution of $(\mathcal{P}_3)$ balancing the total infusion duration of non-critical patients over the days of the planning horizon */

2 Find an optimal solution $(\bar{x}, \bar{y}, \bar{z}^B, \bar{z}^C, \bar{\alpha}^V, \bar{\alpha}^I, \bar{\omega}, \bar{\beta})$ of $(\mathcal{P}_3^b)$

/* Fix the set of patients treated on each day */

3 **for** $d \in D$ **do**

4 $\quad P_d \leftarrow \left\{ p \in P : \sum_{s \in S^V} \bar{x}_{pds} = 1 \right\}$

5 **end**

/* Once the set of patients treated each day is fixed, solve problem $(\mathcal{P}_3)$ by decomposing it into a set of problems one for each day */

6 **for** $\delta \in D$ **do**

7 $\quad$ find an optimal solution of the day δ problem:

$$\begin{cases} \max\limits_{(x,y,z^B,z^C,\alpha^V,\alpha^I,\omega)} & F_3(z^C) \\ \text{subject to} & (1) - (10) \\ & \alpha_\delta^V = \bar{\alpha}_\delta^V \\ & \alpha_\delta^I = \bar{\alpha}_\delta^I \\ & \omega_\delta = \bar{\omega}_\delta \end{cases}$$

$\quad$ where the variables x_{pds}, y_{pds}, z_{pds}^B, z_{pds}^C, α_d^V, α_d^I and ω_d are restricted to $p \in P_\delta$, and $d = \delta$

8 **end**

/* Solve $(\mathcal{P}_3)$ with warm start */

9 Use the union of the solutions found at lines 6–8 as a warm start to solve the whole problem $(\mathcal{P}_3)$

In Section 5.1, we describe the considered instances. Section 5.2 reports the computational results about problem ($\mathcal{P}_1$). Section 5.3 reports the comparison between formulation ($\mathcal{P}_2$) and Procedure 2. The comparison between formulation ($\mathcal{P}_3$) and Procedure 3 is reported in Section 5.4. Finally, the values of the three metrics and the resulting utilization rates of examination rooms, beds and chairs are analyzed in Section 5.5.

5.1. Instances description

To test our approach, we utilize data from San Martino University Hospital in Genoa, Italy. The hospital has recently established an outpatient cancer center for chemotherapy treatment, serving patients from six hematology and oncology departments within the hospital. Six examination rooms are available for clinician visits, along with 26 chairs and 27 beds for infusions, at the center. The center is open from Monday to Friday; thus, we consider a $|D| = 5$ day planning horizon. Each day, the center is open from 8 a.m. to 5 p.m., corresponding to $|N^I| = 54$ time slots, each 10 minutes long. However, the regular visit time is from 8 a.m. to 2 p.m., corresponding to $N^V = 36$ time slots. To allow visits and infusions to start after the regular opening hours, we added two hours of overtime, both for visits and infusions. Thus, we set $|S^I| = 66$ and $|S^V| = 48$.

Our approaches have been tested on a set of 51 instances corresponding to 51 weeks of a year. Each instance specifies the patients to be scheduled in the corresponding week. The weeks with fewer than four working days, due to concurrent national holidays, have been removed from the set of instances. The visit duration v_p is assumed to be deterministic, and it averages 10 minutes for the oncology patients and 20 minutes for the hematology patients, who usually require a more thorough examination by the clinician. The drug administration time f_p ranges from one to four hours, depending on the cancer Macro-Group (cMG).

Patients are grouped into $|K| = 7$ cancer pathologies, or cMGs, adopting the classification reported by the American Joint Committee on Cancer (Amin et al., 2017). One group includes all the patients with hematological cancers (HE) such as leukemia, lymphoma, and myeloma, which represent approximately 30% of the total number of patients treated. The oncology patients are divided into six categories mainly based on the specific body site or organ affected by the cancer: Breast (BR), Gynecology (GY), Lung-respiratory (LU), Gastrointestinal (GI), Urology (UR), and Others (OT).

Table 3 shows the total number of patients $|P|$, the number and percentage of critical patients, the number and percentage of patients for each cMG, and their weekly average, minimum and maximum values, and standard deviation. In the year considered, 31330 chemotherapy treatments were recorded. The number of patients to be scheduled per week ranges from 430 to 719. Critical patients account for approximately 24% of the total number of treatments, although this percentage can reach 37% in some weeks. In terms of the distribution of patients among the cMG, hematological patients (HE) and breast cancer patients (BR) are the most

	$\|P\|$	Critical patients #	Critical patients %	Cancer Macro Groups HE #	HE %	GI #	GI %	UR #	UR %	GY #	GY %	BR #	BR %	OT #	OT %	LU #	LU %
Total	31330	7663	24.46	8713	27.81	3218	10.27	1870	5.97	1102	3.52	8288	26.45	3922	12.52	4217	13.46
Weekly avg	614	150	28.46	171	32.36	63	11.95	37	6.94	22	4.09	163	30.78	77	14.46	83	15.66
Weekly min	430	81	15.34	90	17.05	36	6.82	24	4.55	12	2.27	121	22.92	60	11.36	60	11.36
Weekly max	719	196	37.12	214	40.53	81	15.34	51	9.66	37	7.01	194	36.74	94	17.80	115	21.78
Weekly SD	56	23	4.34	25	4.80	9	1.68	7	1.28	5	1.01	15	2.84	8	1.57	12	2.19

Table 3: Instances patient data.

frequent, accounting for more than 50% of the total number of treatments, in all the weeks. In fact, in four out of 51 instances, this percentage exceeds 70%. The data reported in Table 3 show a limited variation in the distribution of patients in the cMGs between weeks. The largest variation is observed in hematological patients, with a standard deviation of approximately 25 patients. The limited variation in the weekly number of patients is typical for the health service considered in this context. In fact, chemotherapy appointments, especially for solid tumors, are cyclically scheduled according to the treatment plan decided by the oncologist, and adherence to the treatment schedule and the duration of the cycles are of paramount importance for the treatment outcome and effectiveness.

On each day, each examination room is assigned to a single pathology, according to a block scheduling policy. A block is defined by a room $r \in R$ and a working day $d \in D$. The MCP, i.e., the assignment of pathologies to blocks, is assumed to be given; it is defined at the beginning of each month and repeated cyclically over the weeks. We generate the MCP by adapting the approach proposed in Carello et al. (2022) to assign visit blocks to pathologies, ensuring that all patients to be scheduled can be treated. In particular, we allocated the blocks to the pathologies based on the maximum weekly number of requests derived from the historical data, and we optimized each month independently from the others. The number of blocks allocated to each pathology is similar, although not identical, in the different months: between 10 and 12 blocks are allocated to HE, between 2 and 3 to GI, 2 to UR, between 1 and 5 to GY, 5 or 6 to BR, 3 to OT, and 3 or 4 to LU.

In the considered instances, both the MCP and the 51 weekly instances are derived from the same 12-month historical dataset. The MCP is generated from monthly aggregates of that year, whereas the 51 weekly instances are built from the corresponding patient-level data at weekly granularity. Therefore, the numerical results reflect a setting in which the operational demand is consistent with the historical data of the year used to design the MCP, i.e. the demand has not significantly changed over time.

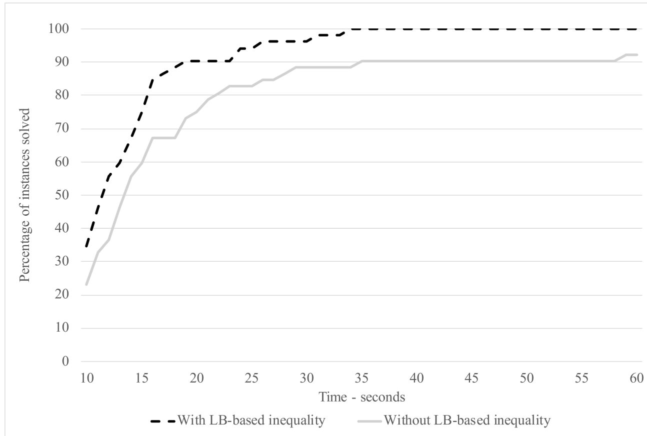

Figure 1: $(\mathcal{P}_1)$ performance profile: evaluating the impact of the LB_1 based inequality.

5.2. Results on problem $(\mathcal{P}_1)$

We evaluate the impact of adding inequality (11), based on the lower bound LB_1, on the CPU time required to solve $(\mathcal{P}_1)$. Figure 1 shows a comparison of the performance profile of the model with and without the additional inequality. The percentage of instances solved in a given time is reported. As shown in the figure, the addition of the inequality significantly improves performance. It allows solving all instances in less than 40 seconds, whereas without inequality (11), it is only possible to solve about 92% of the instances in one minute.

Aggregated details on CPU times are given in Table 4, where the average and maximum CPU time required for solving $(\mathcal{P}_1)$, for computing LB_1, and for solving $(\mathcal{P}_1)$ with the additional inequality are given. Even though both models, with and without the additional inequality, can solve all instances within the 300-second time limit, adding the inequality significantly reduces the computational time. Both the average and maximum CPU time required for solving $(\mathcal{P}_1)$ without the LB_1 additional inequality are significantly higher than those of the model enriched with the additional inequality. The average CPU time without the additional inequality is approximately twice that of the one with it, while adding the inequality reduces the maximum time from more than 4 minutes to about 30 seconds.

	$(\mathcal{P}_1)$ without additional LB_1 inequality	LB_1 computation	$(\mathcal{P}_1)$ with additional LB_1 (including LB_1 time)
average CPU time [s]	23.73	0.29	12.48
maximum CPU time [s]	273.50	14.30	30.84

Table 4: $(\mathcal{P}_1)$ computational time.

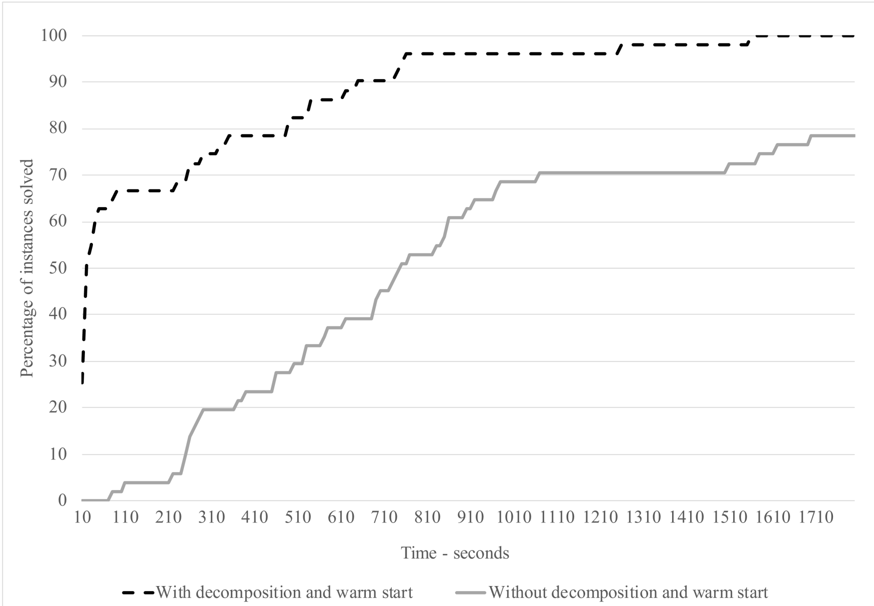

Figure 2: ($\mathcal{P}_2$) performance profile: evaluating the impact of the decomposition-based warm start.

5.3. Results on problem ($\mathcal{P}_2$)

We evaluate the impact of the warm start based on the decomposition heuristic (Procedure 2). The results are shown in Figure 2, which compares the performance profile of the formulation ($\mathcal{P}_2$) with and without the additional decomposition-based warm start. The figure shows the percentage of instances solved in a given time (in seconds). Adding the warm start has a significant impact. In fact, by adding the warm start, we can solve more than 60% of the instances in under one minute and more than 95% in 15 minutes. Instead, without the warm start, the solver cannot solve even 80% of the instances in 30 minutes.

Further details are given in Table 5, where the results of model ($\mathcal{P}_2$), of the decomposition-based heuristic, and of the model with the warm start are compared. The number of instances solved to optimality, the average and maximum CPU times, and the average and maximum absolute gaps to the lower bound are provided for each of the three compared solution methods.

The results clearly show that the model with the warm start outperforms the formulation ($\mathcal{P}_2$). The basic model fails to find an optimal solution in six instances, whereas Procedure 2 solves all instances optimally. In fact, adding the warm start reduces the average CPU time for all instances from about 20 minutes to less than 5 minutes. Furthermore, the maximum CPU time of Procedure 2 is halved with respect to the formulation ($\mathcal{P}_2$), dropping to 1556 seconds. As a consequence of the speedup, adding the warm start improves the quality of the results: it increases the number of instances solved to optimality and reduces the value of the total waiting time objective function. In fact, the lower bound of the waiting time is always 0 for all instances, but the model ($\mathcal{P}_2$) obtains a strictly positive waiting time in

	$(\mathcal{P}_2)$ without warm start	Decomposition heuristic	Procedure 2
# optimal solutions found	45	34	51
average CPU time [s]	1178.86	64.04	208.84
maximum CPU time [s]	3574.05	274.81	1556.59
average absolute gap [time slots]	7.00	1.71	0
max absolute gap [time slots]	11	4	0

Table 5: $(\mathcal{P}_2)$ - Methods comparison: column two reports the results obtained solving $(\mathcal{P}_2)$ without the warm start; column three reports the results obtained by the decomposition heuristic alone; column four reports the results obtained by the Procedure 2 (heuristic and solution of $(\mathcal{P}_2)$ starting from the warm start).

6 instances, ranging from 1 slot to 11 slots, while the Procedure 2 always finds the optimal solution, i.e., it always provides a solution with zero slots of waiting time.

Note that even the decomposition-based heuristic alone exhibits very good performance, as it finds the optimal solution in 34 instances, with an average CPU time of approximately 1 minute. The maximum CPU time is about an order of magnitude smaller than that of the model. Although the heuristic fails to find the optimal solution in more instances (17) than the formulation $(\mathcal{P}_2)$ without warm start (6), it provides smaller average and maximum absolute gaps. Furthermore, the heuristic improves upon the model $(\mathcal{P}_2)$ in 5 instances, while it is worse in 14 instances.

5.4. Results on problem $(\mathcal{P}_3)$

We assess the impact of adding the decomposition-based warm start and the performance of the decomposition heuristic (Procedure 3). Aggregated results are given in Table 6, where the number of optimal solutions found, the number of solutions within a certain gap from the known best Upper Bound (UB), the number of best solutions found (best LB), the average and maximum gap from the best LB, and the CPU times (both average and maximum) are given for each method. Further analysis is provided by Figure 3, which shows the performance profile of the three approaches. The figure shows the percentage of instances within 10% of the best UB achieved within a given CPU time.

The results show that adding the warm start has a significant impact on performance, particularly in terms of the lower bound. In fact, Procedure 3 finds the best solution in all weeks except one. As a consequence, it guarantees the smallest gap w.r.t. the best LB, both on average (0.01%) and maximum (0.47%), while the average and maximum gaps of the model without the warm start increase, up to about 0.1% and 2.5%, respectively. If we focus instead on the gap with respect to the best UB, the behavior of the model with and without the warm start is quite similar: they find the same number of instances within the different percentage gaps considered. The average CPU time of Procedure 3 is about 7 minutes less than that of

	$(\mathcal{P}_3)$ without warm start	Decomposition heuristic	$(\mathcal{P}_3)$ with warm start
# optimal solutions found	9	1	9
# within 2% w.r.t. best UB	28	8	28
# within 5% w.r.t. best UB	41	36	41
# within 10% w.r.t. best UB	45	45	45
# best solutions found (LB)	45	2	50
average percentage gap w.r.t. best LB [%]	0.10	1.55	0.01
maximum percentage gap w.r.t. best LB [%]	2.49	3.80	0.47
average CPU time [s]	6694.26	259.02	6269.11
maximum CPU time [s]	7177.76	494.26	7017.04

Table 6: $(\mathcal{P}_3)$ - Methods comparison.

the model without the warm start. Instead, the decomposition heuristic is significantly faster, taking approximately four minutes on average, and slightly more than eight minutes in the worst case. On the other hand, its performance is worse: it finds the optimal solution only in one instance, and its average gap w.r.t. the best known LB is about 1.55%. Although its performance is inferior to that of the other two approaches, Figure 3 demonstrates that it is a viable alternative when solving $(\mathcal{P}_3)$ requires rapid execution. In fact, the heuristic finds a solution within 10% of the best UB in less than 10 minutes for more than 88% of the instances.

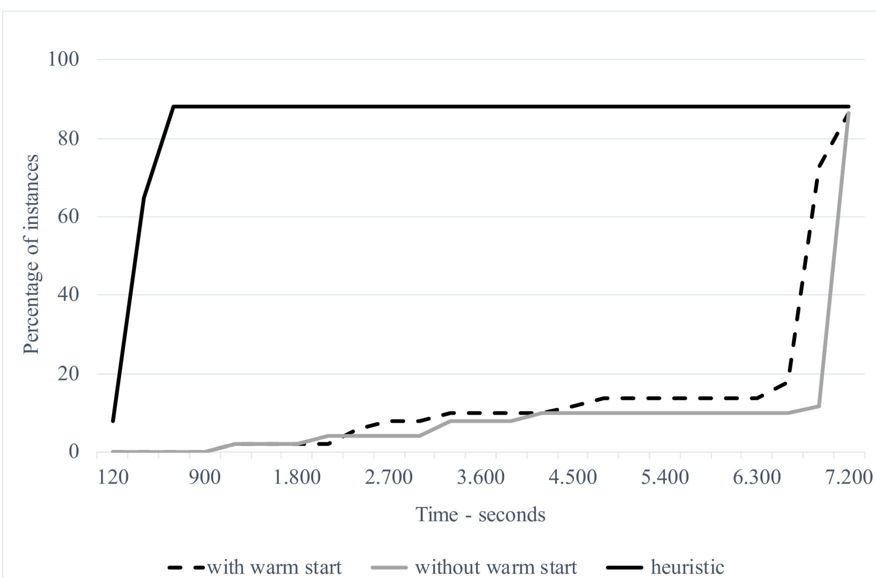

Figure 3: $(\mathcal{P}_3)$ performance profile: percentage of instances within a 10% gap w.r.t. the best UB known found within a given time.

5.5. *Metrics and performance*

Let us now focus on the three metrics considered: overtime F_1, waiting time F_2, and the number of non-critical patients receiving infusions on a chair F_3. The obtained values of the metrics are reported in Table 7. For each week, we report the total number of patients and the number of critical patients to be scheduled; the total overtime over one week in time slots obtained by solving $(\mathcal{P}_1)$; the average waiting time per patient (in time slots) obtained by solving $(\mathcal{P}_1)$ and $(\mathcal{P}_2)$, respectively; the percentage of non-critical patients receiving infusion on a chair obtained by $(\mathcal{P}_1)$, $(\mathcal{P}_2)$, and $(\mathcal{P}_3)$, respectively.

Problem $(\mathcal{P}_1)$ can schedule all patients without overtime in all weeks except three weeks (11, 16, and 17), where the overtime is 8, 8, and 6 slots, respectively, due to national holidays reducing the number of working days (from 5 to 4). The performance is very good as the overtime is at most one hour and 20 minutes, and in a very small number of weeks. Three pathologies require overtime, mostly for visits, while only one pathology requires overtime for infusions, and this is in a single week. The maximum overtime per pathology is one hour for visits and 70 minutes for infusions.

In the optimal solutions of problem $(\mathcal{P}_1)$, the values of the other two metrics are obviously poor since they are not considered in the model. As for the waiting time metric, it is strictly positive in all weeks, with an average of 8.61 time slots and rising to 9.29 time slots in the worst-case scenario. Instead, it is dramatically reduced by solving $(\mathcal{P}_2)$. In fact, in $(\mathcal{P}_2)$ the value of the objective function is equal to 0 in all weeks, providing a very good result. We can therefore infer that the two metrics are not related and that there are many optimal solutions of $(\mathcal{P}_1)$ among which we can select those with the minimum waiting time. A similar remark holds also for the third metric, whose results are also reported in Figure 4. In fact, solving $(\mathcal{P}_3)$ yields an improvement in the third metric of approximately 45% compared to the solutions of $(\mathcal{P}_1)$ and about 40% compared to the solution of $(\mathcal{P}_2)$, selecting among equivalent optima the one that provides significantly better values of the third metric. The improvement may increase to approximately 69% and 65%, respectively, for $(\mathcal{P}_1)$ and $(\mathcal{P}_2)$. It is interesting to note that the values obtained by $(\mathcal{P}_1)$ and $(\mathcal{P}_2)$ are rather similar and that $(\mathcal{P}_1)$ provides a better value in 8 weeks.

Let us now focus on the analysis of the performance with respect to the utilization rate of the resources involved, i.e., examination rooms for visits, chairs, and beds for infusions. In Table 8, the analysis of the utilization of the examination rooms is given. The average, minimum, and maximum % utilization rate, and the number of weeks with a utilization below 50% and 75% are given, as global values and detailed for each pathology. The overall average utilization rate of the examination rooms is 68.52%. Five weeks out of 51 have an utilization rate greater than 75% and the utilization rate is never below 50%. The average utilization of the examination rooms used for different pathologies differs significantly, ranging from 34.8% for pathology GY to 86.89% for pathology HE. The minimum and maximum utilization rates

Instance	# patients total	# patients critical	total overtime [time slots] $(\mathcal{P}_1)$	average waiting time [time slots] $(\mathcal{P}_1)$	average waiting time [time slots] $(\mathcal{P}_2)$	patient preferences met [%] $(\mathcal{P}_1)$	patient preferences met [%] $(\mathcal{P}_2)$	patient preferences met [%] $(\mathcal{P}_3)$
1	528	128	0	9.14	0	64.00	64.25	85.50
2	665	196	0	8.97	0	65.46	66.10	88.91
3	642	176	0	8.27	0	62.66	65.67	89.48
4	554	135	0	8.68	0	60.62	58.95	97.37
5	635	172	0	8.43	0	63.07	61.12	89.20
6	637	182	0	9.16	0	65.71	69.67	93.85
7	656	175	0	8.96	0	64.24	64.24	87.73
8	587	175	0	8.65	0	63.59	66.26	99.27
9	609	156	0	8.22	0	62.69	63.58	93.16
10	687	182	0	8.89	0	63.76	64.95	84.75
11	714	186	8	9.25	0	62.31	64.39	81.25
12	609	168	0	8.67	0	65.31	63.04	95.46
13	658	168	0	8.75	0	59.18	64.29	86.12
14	699	179	0	8.23	0	62.50	64.23	82.69
15	607	140	0	8.60	0	61.03	61.46	92.51
16	588	149	8	8.00	0	61.73	65.60	82.23
17	603	139	6	7.86	0	61.64	63.15	76.94
18	719	179	0	8.09	0	63.89	64.07	80.00
19	591	147	0	8.28	0	58.56	60.81	97.30
20	623	147	0	8.53	0	60.08	62.39	89.08
21	667	169	0	8.70	0	61.45	64.86	86.35
22	655	169	0	9.10	0	63.99	62.35	86.63
23	621	154	0	9.12	0	60.81	64.88	91.01
24	634	149	0	8.94	0	60.00	61.44	86.19
25	608	158	0	8.66	0	61.33	59.11	92.89
26	647	164	0	8.54	0	62.73	67.49	87.99
27	649	140	0	8.94	0	59.72	60.12	83.69
28	606	148	0	8.50	0	60.70	62.01	91.92
29	595	138	0	8.42	0	61.05	63.89	91.68
30	642	141	0	8.80	0	57.88	62.87	85.63
31	585	142	0	7.96	0	59.59	64.33	97.29
32	431	81	0	8.45	0	57.43	63.71	97.43
33	653	153	0	8.78	0	59.00	62.00	84.80
34	608	141	0	8.31	0	60.81	59.10	91.65
35	573	128	0	8.17	0	62.25	63.15	92.36
36	560	108	0	8.09	0	56.19	62.61	91.15
37	583	139	0	7.76	0	59.23	67.79	91.67
38	623	157	0	8.64	0	60.73	61.37	88.84
39	626	162	0	8.60	0	62.93	62.07	91.59
40	602	121	0	8.03	0	58.84	58.84	89.60
41	612	150	0	8.63	0	62.34	66.45	94.37
42	633	163	0	8.61	0	62.34	63.40	90.64
43	539	126	0	8.73	0	61.02	62.47	83.78
44	649	148	0	8.71	0	60.88	60.88	82.24
45	642	162	0	8.42	0	62.08	62.29	85.00
46	557	125	0	8.99	0	60.19	62.27	92.82
47	577	134	0	8.93	0	58.24	60.27	92.55
48	670	148	0	9.29	0	61.30	60.34	82.95
49	617	136	0	8.71	0	58.00	61.33	88.57
50	625	138	0	8.87	0	60.78	64.48	87.06
51	430	92	0	9.05	0	60.65	62.13	76.63
Average	614	150	0.43	8.61	0	61.30	63.11	88.82
Max	719	196	8	9.29	0	65.71	69.67	99.27

Table 7: Instances and results on the three considered metrics. Column 4 reports the total overtime computed solving $(\mathcal{P}_1)$ in time slots; columns 5 and 6 report the average per patient waiting time, based on the solution of $(\mathcal{P}_1)$ and $(\mathcal{P}_2)$, respectively; columns 7, 8, and 9 report the percentage of preferences met for non-critical patients, based on the solution of $(\mathcal{P}_1)$, $(\mathcal{P}_2)$, and $(\mathcal{P}_3)$, respectively.

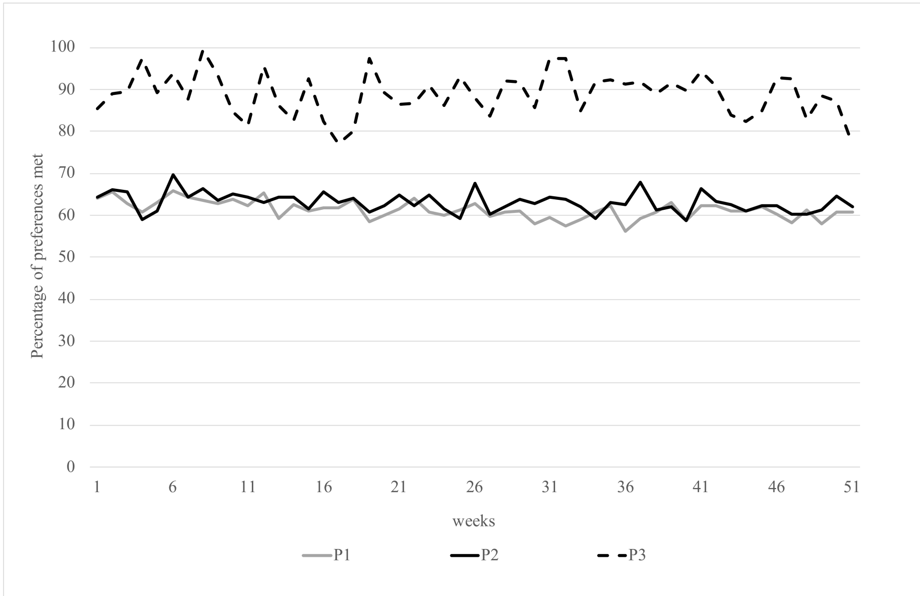

Figure 4: Percentage of patient preferences met in the solution of the three problems.

strongly differ among the pathologies as a result of the availability of examination rooms and clinicians for the patients affected by the different pathologies. Recall that the number of examination rooms available for each pathology per week is fixed by the Master Chemotherapy Planning (MCP) and can be changed only in a longer time frame (3 months). The lack of flexibility in the MCP also generates a high variance between the minimum and maximum utilization rate of the examination rooms for each pathology over the year. As an example of GY pathology, the minimum value in one week is 10.6 and increases to 102.8 in the following week.

Table 9 instead reports the utilization rate of beds and chairs. The utilization rate of the chairs is always greater than the utilization rate of the beds. The utilization rate of beds is considerably lower, 43.7% on average, with a minimum value of 24.6%. Even if the objective function of the third problem aims at maximizing the utilization of the chairs for

		Pathology						
	Global	HE	GI	UR	GY	BR	OT	LU
Average utilization [%]	68.52	86.89	72.44	54.20	34.80	83.37	74.28	73.69
Minimum utilization [%]	56.96	62.50	45.40	36.10	10.60	63.90	59.30	43.10
Maximum utilization [%]	85.89	99.50	100.00	108.30	102.80	106.90	115.30	97.20
# weeks below 50%	0	0	1	21	39	0	0	1
# weeks below 75%	46	7	28	49	46	9	30	29

Table 8: Examination rooms utilization rate: per pathology analysis.

	Average [%]	Minimum [%]	Maximum [%]	# weeks below 50%	# weeks below 75%
Beds	43.72	24.60	64.10	41	51
Chairs	78.10	75.50	81.50	0	0

Table 9: Beds and chairs utilization rate.

meeting patient preferences, the average utilization rate of the chairs never exceeds 81.5%. These utilization levels are consistent with those reported in similar studies on outpatient chemotherapy centers (Hesaraki et al., 2019; Mandelbaum et al., 2020; Karakaya et al., 2023), where average rates between 60% and 80% are observed depending on the patient mix and treatment duration variability.

6. Conclusions

We addressed the simultaneous interday and intraday chemotherapy planning and multi-appointment scheduling problem in a shared cancer center. We considered three different metrics that take into account both management and patient perspectives. As the three objectives are hierarchical, we tackle the resulting multi-objective problem by solving each of the three problems in sequence. Improved formulations, heuristics, and warm starts have been developed to speed up the solution process. These approaches outperform state-of-the-art solvers, enabling the obtainment of very high-quality solutions in reasonable computational times.

The results show that the framework can schedule all patients with minimal or no overtime. Surprisingly, examination rooms remain the bottleneck resource. Although some imbalance is expected due to the MCP structure, the extent of the variation across pathologies was greater than anticipated, suggesting that more flexible resource allocation policies could further improve performance. Indeed, tackling intraday and interday scheduling simultaneously achieves good performance in terms of room, bed, and chair utilization rates; the utilization rate of exam rooms is not balanced across pathologies. This suggests that more flexible resource allocation policies could accommodate an even greater number of requests, which are expected to increase in the future. We therefore suggest exploring more flexible policies and their impact as a future development. Additionally, we believe that jointly designing the MCP and the appointment scheduling, possibly including additional limited resources such as nurses, could lead to further improvements and extensions in the management of the cancer center. Finally, the inherent uncertainty of patients' clinical conditions may prevent some from receiving infusion treatments on their assigned appointment date. The deviation of actual infusion durations from the planned ones may also affect the feasibility and robustness of the daily schedule. These uncertainty issues are worthy of in-depth investigation.

Acknowledgements

The authors would like to thank the anonymous Reviewers for their careful reading, insightful comments, and valuable suggestions that helped us improve the quality of the manuscript. The authors gratefully acknowledge the Cancer Center of the San Martino Public Hospital in Genoa, Italy, for sharing the key elements of the problem and the operating scenario, as well as for providing the real data to testing the approaches developed.
M. Passacantando is a member of the Gruppo Nazionale per l'Analisi Matematica, la Probabilità e le loro Applicazioni (GNAMPA – National Group for Mathematical Analysis, Probability and their Applications) of the Istituto Nazionale di Alta Matematica (INdAM – National Institute of Higher Mathematics).

References

Abdulrashid, I., Delen, D., Usman, B., Uzochukwu, M. I., & Ahmed, I. (2024). A multi-objective optimization framework for determining optimal chemotherapy dosing and treatment duration. *Healthcare Analytics*, 5, Article 100335. `https://doi.org/10.1016/j.health.2024.100335`

Agnetis, A., Bianciardi, C., & Iasparra, N. (2019). Integrating lean thinking and mathematical optimization: A case study in appointment scheduling of hematological treatments. *Operations Research Perspectives*, 6, Article 100110. `https://doi.org/10.1016/j.orp.2019.100110`

Agur, Z., Hassin, R., & Levy, S. (2006). Optimizing chemotherapy scheduling using local search heuristics. *Operations Research*, 54(5), 829–846. `https://doi.org/10.1287/opre.1060.0320`

Ahmadi-Javid, A., Jalali, Z., & Klassen, K. J. (2017). Outpatient appointment systems in healthcare: A review of optimization studies. *European Journal of Operational Research*, 258(1), 3–34. `https://doi.org/10.1016/j.ejor.2016.06.064`

Amin, M., Edge, S., Greene, F. L., Byrd, D. R., Brookland, R. K., Washington, M. K., Gershenwald, J. E., Compton, C. C., Hess, K. R., Sullivan, D. C., Jessup, J. M., Brierley, J. D., Gaspar, L. E., Schilsky, R. L., Balch, C. M., Winchester, D. P., Asare, E. A., Madera, M., Gress, D. M., & Meyer, L. R. (2017). *American Joint Committee on Cancer (AJCC) Cancer Staging Manual, Eighth edition*. Springer.

Bazrafshan, N. & Lam, S. S. (2025). Outpatient chemotherapy planning and decision making: a systematic review. *Health Systems*, 1–34. `https://doi.org/10.1080/20476965.2025.2556061`

Benzaid, M., Lahrichi, N., & Rousseau, L. (2020). Chemotherapy appointment scheduling and daily outpatient-nurse assignment. *Health Care Management Science*, 23(1), 34–50. https://doi.org/10.1007/s10729-018-9462-6

Bray, F., Laversanne, M., Sung, H., Ferlay, J., Siegel, R. L., Soerjomataram, I., & Jemal, A. (2024). Global cancer statistics 2022: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*, 74(3), 229–263. https://doi.org/10.3322/caac.21834

Carello, G., Landa, P., Tanfani, E., & Testi, A. (2022). Master chemotherapy planning and clinicians rostering in a hospital outpatient cancer centre. *Central European Journal of Operations Research*, 30, 159–187. https://doi.org/10.1007/s10100-021-00786-x

Cataldo, A., Sufan, S., Lorca, A., Andresen, M., Sánchez, C., & Sauré, A. (2023). Multi–stage process for chemotherapy scheduling and effective capacity determination. *International Transactions in Operational Research*, 30(1), 151–180. https://doi.org/10.1111/itor.13117

Celik, B., Gul, S., & Karsu, O. (2025). Maintaining fairness in stochastic chemotherapy scheduling. *Omega*, 137, Article 103338. https://doi.org/10.1016/j.omega.2025.103338

Corsini, R. R., Costa, A., Fichera, S., & Parrinello, V. (2022). Hybrid harmony search for stochastic scheduling of chemotherapy outpatient appointments. *Algorithms*, 15(11), Article 424. https://doi.org/10.3390/a15110424

Debela, D., Muzazu, S., Heraro, K., Ndalama, M., Mesele, B., Haile, D., Kitui, S., & Manyazewal, T. (2021). New approaches and procedures for cancer treatment: Current perspectives. *SAGE Open Medicine*, 9, 1–10. https://doi.org/10.1177/20503121211034366

Garaix, T., Rostami, T., & Xie, X. (2020). Daily outpatient chemotherapy appointment scheduling with random deferrals. *Flexible Services and Manufacturing Journal*, 32, 129–153. https://doi.org/10.1007/s10696-018-9326-x

Gul, S. (2024). Nursing care flexibility in chemotherapy appointment scheduling. *Flexible Services and Manufacturing journal*, 36, 918–945. https://doi.org/10.1007/s10696-023-09526-6

Hadid, M., Elomri, A., Mekkawy, T. E., Jouini, O., Kerbache, L., & Hamad, A. (2022a). Operations management of outpatient chemotherapy process: An optimization-oriented comprehensive review. *Operations Research Perspectives*, 9, Article 100214. https://doi.org/10.1016/j.orp.2021.100214

Hadid, M., Elomri, A., Padmanabhan, R., Kerbache, L., Jouini, O., El Omri, A., Nounou, A., & Hamad, A. (2022b). Clustering and stochastic simulation optimization for outpatient chemotherapy appointment planning and scheduling. *International Journal of Environmental Research and Public Health*, 19(23), Article 15539. https://doi.org/10.3390/ijerph192315539

Han, Y., Johnson, M. E., Shan, X., & Khasawneh, M. (2024). A multi-appointment patient scheduling system with machine learning and optimization. *Decision Analytics Journal*, 10, Article 100392. https://doi.org/10.1016/j.dajour.2023.100392

Hesaraki, A., Dellaert, N., & de Kok, T. (2019). Generating outpatient chemotherapy appointment templates with balanced flowtime and makespan. *European Journal of Operational Research*, 275(1), 304–318. https://doi.org/10.1016/j.ejor.2018.11.028

Hesaraki, A., Dellaert, N., & de Kok, T. (2020). Integrating nurse assignment in outpatient chemotherapy appointment scheduling. *OR Spectrum: Quantitative Approaches in Management*, 42, 935–963. https://doi.org/10.1007/s00291-020-00596-8

Hesaraki, A., Dellaert, N., & de Kok, T. (2023). Online scheduling using a fixed template: the case of outpatient chemotherapy drug administration. *Health Care Management Science*, 26(1), 117–137. https://doi.org/10.1007/s10729-022-09616-1

Heshmat, M. & Eltawil, A. (2021). Solving operational problems in outpatient chemotherapy clinics using mathematical programming and simulation. *Annals of Operations Research*, 298, 289–306. https://doi.org/10.1007/s10479-019-03500-y

Heshmat, M., Nakata, K., & Eltawil, A. (2018). Solving the patient appointment scheduling problem in outpatient chemotherapy clinics using clustering and mathematical programming. *Computers & Industrial Engineering*, 124, 347–358. https://doi.org/10.1016/j.cie.2018.07.033

Hooshangi-Tabrizi, P., Contreras, I., Bhuiyan, N., & Batist, G. (2020). Improving patient-care services at an oncology clinic using a flexible and adaptive scheduling procedure. *Expert Systems with Applications*, 150, Article 113267. https://doi.org/10.1016/j.eswa.2020.113267

Issabakhsh, M., Lee, S., & Kang, H. (2021). Scheduling patient appointment in an infusion center: a mixed integer robust optimization approach. *Health Care Management Science*, 24(1), 117–139. https://doi.org/10.1007/s10729-020-09519-z

Karakaya, S., Gul, S., & Çelik, M. (2023). Stochastic scheduling of chemotherapy appointments considering patient acuity levels. *European Journal of Operational Research*, 305(2), 902–916. https://doi.org/10.1016/j.ejor.2022.06.014

Keshtzari, M. & Norman, B. A. (2024). Capacity allocation in cancer centers considering demand uncertainty. *Sci*, 6(2), Article 22. https://doi.org/10.3390/sci6020022

Lamé, G., Jouini, O., & Stat-Le-Cardinal, J. (2016). Outpatient chemotherapy planning: A literature review with insight from a case study. *IIE Transactions on Healthcare System Engineering*, 6(3), 127–139. https://doi.org/10.1080/19488300.2016.1189469

Liang, B. & Turkan, A. (2016). Acuity-based nurse assignment and patient scheduling in oncology clinics. *Health Care Management Science*, 19, 207–226. https://doi.org/10.1007/s10729-014-9313-z

Lyon, G., Cataldo, A., Angulo, G., Rey, P. A., & Sauré, A. (2022). A column generation approach to intraday scheduling of chemotherapy patients. *International Journal of Production Research*, 61(7), 2231–2249. https://doi.org/10.1080/00207543.2022.2067505

Mandelbaum, A., Momčilović, P., Trichakis, N., Kadish, S., Leib, R., & Bunnell, C. A. (2020). Data-driven appointment-scheduling under uncertainty: The case of an infusion unit in a cancer center. *Management Science*, 66(1), 243–270. https://doi.org/10.1287/mnsc.2018.3218

Marynissen, J. & Demeulemeester, E. (2020). Literature review on multi-appointment scheduling problems in hospital settings. *European Journal of Operational Research*, 272, 407–419. https://doi.org/10.1016/j.ejor.2018.03.001

Ozyuksel, E., Gul, S., Ünlüyurt, T., & Celik, B. (2025). Coordinating oncologist appointments with chemotherapy treatments under uncertainty. *Computers & Industrial Engineering*, 204, Article 111123. https://doi.org/10.1016/j.cie.2025.111123

Pinedo, M. L. (2022). *Scheduling: Theory, algorithms, and systems*. Springer Cham.

Rezaeiahari, M. & Khasawneh, M. T. (2017). An optimization model for scheduling patients in destination medical centers. *Operations Research for Health Care*, 15, 68–81. https://doi.org/10.1016/j.orhc.2017.09.004

Saville, C., Smith, H., & Bijak, K. (2019). Operational research techniques applied throughout cancer care services: a review. *Health Systems*, 8(1), 52–73. https://doi.org/10.1080/20476965.2017.1414741

Sbeity, H. & Younes, R. (2015). Review of optimization methods for cancer chemotherapy treatment planning. *Journal of Computer Science & Systems Biology*, 8, 74–95. https://doi.org/10.4172/jcsb.1000173

Shi, J., Alagoz, O., Safa, Erenay, F., & Su, Q. (2014). A survey of optimization models on cancer chemotherapy treatment planning. *Annals of Operations Research*, 221, 331–356. https://doi.org/10.1007/s10479-011-0869-4

Siegel, R. L., Giaquinto, A. N., & Jemal, A. (2024). Cancer statistics, 2024. *CA: A Cancer Journal for Clinicians*, 74(1), 12–49. https://doi.org/10.3322/caac.21820

Slocum, R. F., Jones, H. L., Fletcher, M. T., McConnell, B. M., Hodgson, T. J., Taheri, J., & Wilson, J. R. (2021). Improving chemotherapy infusion operations through the simulation of scheduling heuristics: a case study. *Health Systems*, 10(3), 163–178. https://doi.org/10.1080/20476965.2019.1709908

Uttpal, A., Abhijit, D., Arvind, K. S. C., Rupa, S., Amarnath, M., Devendra, K. P., Valentina, D. F., Arun, U., Ramesh, K., Anupama, C., Jaspreet, K. D., Saikat, D., Jayalakshmi, V., & José, M., P. d. l. L. (2023). Cancer chemotherapy and beyond: Current status, drug candidates, associated risks and progress in targeted therapeutics. *Genes & Diseases*, 10(4), 1367–1401. https://doi.org/https://doi.org/10.1016/j.gendis.2022.02.007

van Harten, W. H. (2014). Comprehensive cancer centres based on a network: the OECI point of view. *Ecancermedicalscience*, 8, Article ed43. https://doi.org/10.3332/ecancer.2014.ed43

Wenzel, A., Sauré, A., Cataldo, A., Rey, P. A., & Sánchez, C. (2024). An approximate dynamic programming approach to network-based scheduling of chemotherapy treatment sessions. *International Journal of Production Research*, 62(12), 4314–4330. https://doi.org/10.1080/00207543.2023.2259502

Wilson, B. E., Jacob, S., Yap, M. L., Ferlay, J., Bray, F., & Barton, M. B. (2019). Estimates of global chemotherapy demands and corresponding physician workforce requirements for 2018 and 2040: a population-based study. *The Lancet Oncology*, 20(6), 769–780. https://doi.org/10.1016/S1470-2045(19)30163-9

World Health Organization (2020). WHO report on cancer: setting priorities, investing wisely and providing care for all. Technical report, World Health Organization. https://www.who.int/publications/i/item/9789240001299