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ORIGINAL ARTICLE

A mathematical optimization model for efficient assignment of inpatients in an oncology center in China

Ming Lv[1], Bo Kou[1,2], Zhi-Li Zhou[1] Wen-Bo He[3]

[1]School of Management, Xi'an JiaoTong University, Xi'an, 710049, China; [2]The First Affiliated Hospital of Xi'an JiaoTong University, Department of Cardiovascular Surgery, Xi'an, 710061, China; [3]Medical School, Xi'an JiaoTong University, Xi'an, 710061, China

Summary

This paper addresses a problem for assignment of chemo-receiving inpatients in an oncology care center, which has not been addressed in the literature. Chemotherapy is regarded as one of the most effective treatments for cancer. In recent years, as cancer incidence increased, the number of patients admitted to a cancer treatment center has also been rising. How to balance the workload of medical service resources by planning admission of patients has become an essential problem that must be given consideration by policy-makers. The allocation of chemotherapy patients, different from that of the routine inpatients, is restrained by treatment agreements of patients and presents periodic features. Therefore, the allocation of chemotherapy patients is much more difficult than that of routine patients. A mixed integer programming (MIP) model was first formulated for this problem in order to maximize the usage of beds. Specific features of chemotherapy, such as chemotherapy protocols, were integrated into this model. The inpatient assignment problem was proved to be non-deterministic polynomial-complete and we propose an exact method to solve it. Numerical experiments on suitable use-case scenarios and a practical Chinese oncology center were performed to test and evaluate this model. The obtained results demonstrated the effectiveness of our method. Some useful managerial implication are provided for policy-makers through the analysis of obtained results. The models and methods suggested here can be effectively applied in similar departments of other countries and regions.

Key words: *inpatient assignment, mix integer programming, oncology*

Introduction

According to the 2014 WHO World Cancer Report, cancer morbidity and mortality have continued to increase. The global incidence of cancer has increased by 11% in the past 4 years. By 2012, there were 14.1 million cancer patients and the number of deaths due to cancer had reached 8.2 million. In 2012, half of the new worldwide cancer cases occurred in Asia and mostly in the Chinese mainland, making China's cancer incidence number one in the world. As a result, the number of patients in Chinese oncology care centers has risen dramatically. As it is impractical to quickly upgrade medical facilities, policy-makers of oncology care centers should consider improving their services efficiency to meet the needs of the increasing number of patients.

Chemotherapy is recognized as one of the most effective methods for treating cancer. The purpose of chemotherapy is to kill tumor cells with chemical drugs and prevent them from spreading and dividing. The common ways to deliver chemotherapy are orally and through infusion. Some cancer patients start and finish their chemotherapy sessions within a single day while others must

Correspondence to: Bo Kou, MD, PhD. The First Affiliated Hospital of Xi'an Jiaotong University, No.277, Yanta West street, Yanta district, Xi'an, Shaaanxi province, China. Tel: +86 29 85323338, E-mail: npl117737@163.com
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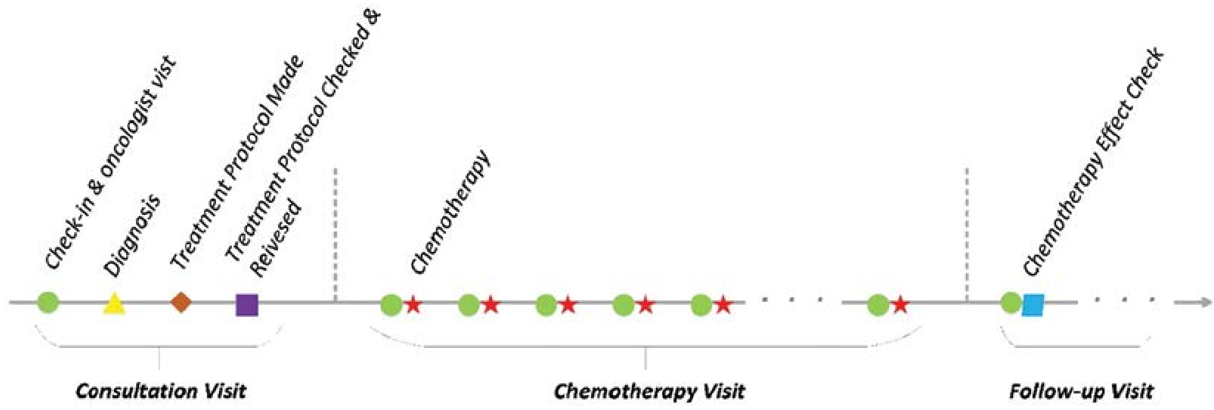

Figure 1. Treatment pathway for inpatient receiving chemotherapy.

stay in oncology care centers for several days to complete treatment. In China, because of the medical insurance system and underdeveloped community medical service, there are more patients in the latter situation than in Western countries. Therefore, whether the oncology care center has enough beds and can use them efficiently to meet the hospitalization demands of chemo-receiving inpatients has become a critical issue.

Figure 1 shows a typical treatment pathway for an inpatient receiving chemotherapy. The patient is assigned to an attending physician for diagnosis on first visit. If the physician determines chemotherapy is required, a chemotherapy protocol according to the patient's condition (including age and physical condition) will be prescribed. The chemotherapy protocol will be sent to a panel of experts headed by a chief physician for review and modification. Once a chemotherapy protocol is finalized, the patient will receive it as planned. The patient is required to be hospitalized on days specified by the protocol. After the course of chemotherapy is completed, the oncology care center will assess its effect and decide the next step in treatment accordingly.

A chemotherapy protocol specifies when and how the chemotherapy is given. The chemotherapy protocol adopted varies, based on the type of cancer and the specific condition of the patient. Moreover, there may be multiple choices of chemotherapy for one type of cancer and the same chemotherapy protocol can be given in different manners. Table 1 lists typical chemotherapy protocols for several common cancers. For example, if the attending physician adopts the etoposide, leucovorin, 5-fluorouracil (ELF) protocol of gastric cancer to treat a patient, the patient will receive a total of 6 to 8 courses of chemotherapy. In between 2 courses, the patient will take a break of 28 days for recovery. In each course, the patient will receive infusion of 3

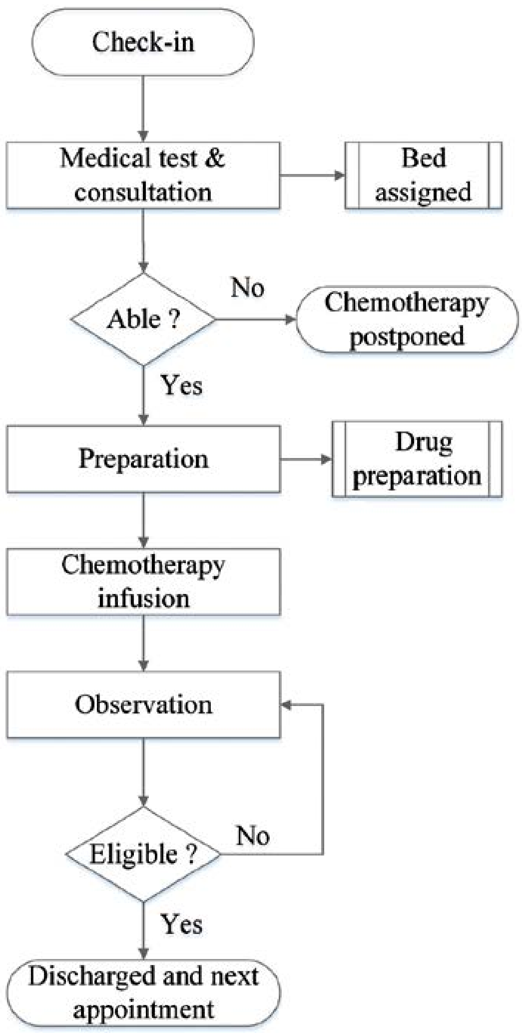

Figure 2. Care process of a chemotherapy session.

drugs from day 2 until day 4. The length of stay in oncology care centers is 3 days starting from enrollment on day 1 to day 3.

As shown in Table 1, chemotherapy proceeds at intervals with a break between each course. This implies the patient comes to the oncology care center in regular cycles. Therefore, a chemotherapy protocol defines a treatment course, which contains several sessions. Figure 2 shows the care process of a typical chemotherapy session. For example, the patient is required to complete the enrollment formalities the day before chemotherapy. Oncology care centers assign a ward number (bed) to the patient if needed and make preparations for chemotherapy. Then, the patient undergoes a comprehensive health check, including blood tests, computed tomography, and X-ray. The attending physician will decide whether the patient is eligible for chemotherapy according to the results and his present condition. If the results permit, the patient will begin chemotherapy under the supervision of the attending physician or a resident doctor. After a treatment process is completed, the patient will temporarily be kept under observation before being discharged. After, the patient is required to come to the oncology care center for the next session according to the chemotherapy protocol.

Therefore, once the chemotherapy start date is known, all subsequent hospital dates for a patient are known. In most cases, a finalized chemotherapy protocol is almost unchangeable. Some chemotherapy protocols are carried out successively such as the ELF protocol for gastric cancer while some require the patient to be hospitalized on discrete dates in a single cycle such as the streptozocin, mitomycin C, and 5-FU (SMF) protocol for pancreatic cancer.

For inpatient assignment, oncology care centers are facing the challenge of the growing number of inpatients and the complex bed capacity requirements caused by diverse chemotherapy protocols. For example, beds are placed in individual wards and at the discretion of various departments. To further complicate the matter, patients should stay on the same bed during chemotherapy sessions, each of which may include consecutive hospitalization days. Therefore, there is an urgent need to devise a highly efficient inpatient assignment strategy for oncology care centers by using management science methods. This is the focus of the present manuscript. To our knowledge, this problem has not been addressed previously. This research was performed in close collaboration with the oncology care center of the First Affiliated Hospital of Xi'an JiaoTong University (FAHOXJTU).

This paper is organized as follows: In the next section, the review of related literature is presented. Section 3 provides a mixed integer programming formulation for the problem. Numerical results are outlined in Section 4. Finally, a summary of the research is given in Section 5.

Literature review

In this section, we present relevant research in the areas of appointment scheduling and in particular management science/operation research applied to oncology care centers.

Appointment scheduling

There have been reports on appointment scheduling. Cayirli et al. [1] and Gupta et al. [2] presented general problem formulation and modeling considerations, and provided taxonomy of methodologies used in previous works. The earliest study was from Bailey [3] who focused on patient waiting time and the time which a consultant may waste waiting for the next patient. Rising et al. [4] presented a case study on the use of mathematical-computer models in developing operating policies for a university health service outpatient clinic. In the study by Brahimi and Worthington [5], queuing models were applied to design an appropriate appointment system for the outpatient department at the Royal Lancaster Infirmary. Klassen and Ruhleder [6] compared various scheduling rules in order to minimize the waiting time of patients as well as the idle time of the service provider. Liu and Liu [7] developed a block appointment system for clinic operations with multiple random arriving doctors. Denton and Gupta [8] studied the problem of the determination of optimal appointment times for a sequence of jobs with uncertain durations. Cayirli et al. [9] used patient and doctor-related measures to assess ambulatory care performance and investigated the interactions among appointment system elements and patient panel characteristics. Robinson and Chen [10] compared two types of appointment-scheduling policies for single providers (traditional and open-access) and found that the open-access scheduling significantly outperformed traditional scheduling. Erdogan and Denton [11] proposed models for scheduling a stochastic server in the presence of uncertainty in demand for appointment requests. Zacharias and Pinedo [12] studied an overbooking model for scheduling arrivals at a medical facility under no-show behavior, with patients having different no-show probabilities and different weights. The results showed that the no-show rate and patient heterogeneity had a significant impact on the optimal schedule and should be taken under consideration.

Management Science/Operation Research applied to oncology care centers

Studies on MS/OR applied to oncology care centers have been scarce. Matta and Patterson [13] provided a multi-dimensional performance measurement framework for an oncology care center by which managers could compare several operationally different outpatient systems across multiple performance measurement dimensions. Conforti et al. [14,15] proposed radiotherapy planning models in order to reduce waiting times and waiting lists for radiotherapy treatments. Santibáñez et al. [16] developed a simulation model to reduce patient waiting time and improve resource utilization at the British Columbia Cancer Agency (BCCA)'s ambulatory care unit. Sauré et al. [17] formulated and solved a discounted infinite-horizon Markov decision process for scheduling cancer treatments in radiation therapy units, also based on medical practice at BCCA. The main purpose of their research was to identify good policies for allocating available treatment capacity to incoming demand, while reducing waiting times in a cost-effective manner.

As for chemotherapy planning and scheduling, Turkcan et al. [18] developed mathematical programming models to solve the chemotherapy operations planning and scheduling problems. However, their main objective was to balance the acuity of patients serviced by a particular nurse as opposed to maximizing utilization. In addition, only four types of cancer were considered, and the number of computation instances was very small. Hahn-Goldberg et al. [19] addressed dynamic uncertainty arising from requests for appointments that arrive in real time and uncertainty caused by last-minute scheduling changes. They proposed dynamic template scheduling, a novel technique that combines proactive and online optimization, and applied it to chemotherapy outpatient scheduling. Sadki et al. [20-22] presented a scheme of planning oncologists for chemotherapy of cancer patients at ambulatory care units. Heuristic methods were used for determining good medical planning in reasonable computational time.

However, Sadki et al. only considered patients who could start and finish their chemotherapy session within one weekday, but excluded chemotherapy receiving inpatients. Besides the fact that health care systems differ in each country (China's medical insurance covers expenses only when the patient is hospitalized), some patients need to be hospitalized during their sessions (for various reasons, such as poor health condition and specific requirements of a chemotherapy protocol). If this is left unconsidered, then the bed demand arising from different chemotherapy protocols may be combined to cause uneven distribution of beds over time, or worse, lead to "bed crisis" on certain days. Therefore, it is highly necessary to consider the chemotherapy of inpatients. This represents the biggest difference between our work and other studies.

Our research also shares some similarities with the resource constrained project scheduling problem with minimal and maximal time-lags (RCPSP/max). Similarly, we are given multiple activities under the constraints of limited resources and seek to start them within a time window. However, the problem we address is different because the RCPSP/max problem has clearly defined precedence constraints while our research does not. Furthermore, oncology care center bed demand occurs periodically, meaning that certain activities restart. The diverse chemotherapy protocols added to the complexity of the problem make it completely different from existing models.

Mathematical model

1. Sets

$\boldsymbol{P}$	Set of patients that have already begun the treatment course, denoted by $\boldsymbol{p}$
$\boldsymbol{I}$	Waiting list of unscheduled patients ready to start the treatment course, denoted by $\boldsymbol{i}$
$\boldsymbol{J}$	Set of wards, denoted by, $\boldsymbol{p}$
$\boldsymbol{H}$	Set of days in the time horizon, denoted by, $\boldsymbol{t}$
$\boldsymbol{T}$	Set of days in the scheduling period, denoted by $\boldsymbol{t}, \boldsymbol{T} \in \boldsymbol{H}$
$\boldsymbol{W}$	Set of weeks in the scheduling period, denoted by $\boldsymbol{w}$
$\boldsymbol{K}$	Set of chemotherapy protocols, denoted by $\boldsymbol{k}$
$\boldsymbol{K'}$	Set of chemotherapy protocols requiring consecutive hospitalized days within a session, denoted by $\boldsymbol{k}, \boldsymbol{K'} \in \boldsymbol{K}$
$\boldsymbol{HD\{k\}}$	Set of hospitalized days of protocol $\boldsymbol{k}$ within a treatment course, denoted by $\boldsymbol{d}$

2. Hypothesis

Based on clinical practice, the following assumptions are made for our problem:

Assumption 1: Monday is the first day of a time horizon.

Assumption 2: We assign ward numbers instead of specific beds to patients.

Assumption 3: The time horizon is $|\boldsymbol{H}|$ while the scheduling period is $|\boldsymbol{T}|$, and $\boldsymbol{T}$ is a subset of $\boldsymbol{H}$. We consider $\boldsymbol{H}$ because some of the current inpatients will occupy beds in the future. When determining inpatient assignment strategy, we only need to consider a short period T.

Assumption 4: A scheduling period of T is considered and the set BP and WP both booked patients and waiting patients in this period are assumed to be known. Each newly admitted patient starts treatment at a given time window according to a given chemotherapy protocol.

In clinical practice, inpatient assignment decision takes place at intervals instead of on a daily basis. Upon each decision epoch, information about newly and previously admitted patients and their chemotherapy protocols are already known. The time window of newly admitted patients and the currently unoccupied beds are also known. Therefore, our study is well applicable to clinical practice.

Assumption 5: For all $K' \in K$, their minimum interval between two consecutive sessions is no less than $|T|$. This assumption simplifies the inpatient assignment problem and rules out the possibility of two consecutive stays during one scheduling. In practice, this assumption is reasonable, because the minimum interval between sessions of all chemotherapy protocols involving consecutive stays in a single cycle is 14 days. Therefore, we can easily make an assignment of inpatients on a weekly basis.

Assumption 6: Every day, each patient is assigned one bed at most. Patients in the set BP are definitely assigned a bed for their treatment. Their treatment information is already known. They all show up (no-show rate is zero) and receive treatment as scheduled. Patients in the set WP have the same priority. If we assume that some of the waiting patients need to start treatment immediately, then we can assume them to be BP.

3. Parameters

Input parameters:

$PRT_{i/p}$	Chemotherapy protocol of patient i/p
SD_p	Start day of booked patient p
C_{jt}	Capacity of ward j on day t
e_i	Earliest hospitalized day of patient i
l_i	Latest hospitalized day of patient i

Parameters obtained from input parameters:

BQH_p	Total hospitalized days of booked patient p
WQH_i	Total hospitalized days of waiting patient i

4. Decision variables

$$x_{pjt} = \begin{cases} 1, \text{if patient } p \text{ is hopitalized in ward } j \text{ on day } t \\ 0, \text{otherwise} \end{cases}$$

$$y_{ijt} = \begin{cases} 1, \text{if patient } i \text{ is hopitalized in ward } j \text{ on day } t \\ 0, \text{otherwise} \end{cases}$$

$$z_{ijt} = \begin{cases} 1, \text{if patient } i \text{ starts chemotherapy in ward } j \text{ on day } t \\ 0, \text{otherwise} \end{cases}$$

$$\sum_{j=1}^{|J|} x_{pjt} \le 1 \quad \forall p, \forall t \quad \{1\}$$

$$\sum_{j=1}^{|J|} y_{ijt} \le 1 \quad \forall i, \forall t \quad \{2\}$$

$$\sum_{t=e_i}^{\min(l_i,|T|)} \sum_{j=1}^{|J|} z_{ijt} \le 1 \quad \forall i \quad \{3\}$$

$$\sum_{t=1}^{e_i-1} \sum_{j=1}^{|J|} z_{ijt} = 0 \quad \forall i \in \{e_i > 1\} \quad \{4\}$$

$$\sum_{t=l_i+1}^{|T|} \sum_{j=1}^{|J|} z_{ijt} = 0 \quad \forall i \in \{l_i < |T|\} \quad \{5\}$$

$$\sum_{p=1}^{|P|} x_{pjt} + \sum_{i=1}^{|I|} y_{ijt} \le C_{jt} \quad \forall j, \forall t \quad \{6\}$$

$$\sum_{p=1}^{|P|} x_{pjt} + \sum_{i=1}^{|I|} z_{ijt} \le C_{jt} \quad \forall j, \forall t \in \{1, \ldots, |T|\} \quad \{7\}$$

$$\sum_{w=1}^{|T|/7} \sum_{7*w-2}^{7*w-1} z_{ijt} = 0 \quad \forall i, \forall j \quad \{8\}$$

$$x_{pjt} \le x_{pjSD_p} \quad \forall p, \forall j, \forall t = \{SD_p, \ldots |T|\} \quad \{9\}$$

$$y_{ijt} \le \sum_{t=e_i}^{\min(l_i,|T|)} z_{ijt} \quad \forall i, \forall j, \forall t \quad \{10\}$$

$$\sum_{j=1}^{|J|} x_{pj(SD_p+d-1)} = 1 \quad \forall p, \forall d \in HD\{PRT_p\} \quad \{11\}$$

$$\sum_{j=1}^{|J|} z_{ijt} \le \sum_{j=1}^{|J|} y_{ij(t+d-1)} \quad \forall i, \forall t \in \{e_i, \ldots, \min(l_i, |T|)\}, \forall d \in HD\{PRT_i\} \quad \{12\}$$

$$\sum_{j=1}^{|J|} \sum_{t=1}^{|H|} x_{pjt} = BQH_p \quad \forall p \quad \{13\}$$

$$\sum_{j=1}^{|J|} \sum_{t=1}^{|H|} y_{ijt} = WQH_i \sum_{t=e_i}^{\min(l_i,|T|)} \sum_{j=1}^{|J|} z_{ijt} \quad \forall i \quad \{14\}$$

$$x_{pjt}, y_{ijt}, z_{ijt} \in (0,1) \quad \{15\}$$

$$SD_p, BQH_p, WQH_i, C_{jt}, \quad e_i, l_i \in N \quad \{16\}$$

Constraints {1} and {2} specify that each patient can be in at most one ward every day. Constraints {3}-{5} ensure that each patient can start chemotherapy at most once in the scheduling horizon and the start day must be within the time window. Constraints {6} and {7} mean that the number of inpatients in a ward will not exceed the ward's capacity. Constraint {8} guarantees that the patient's first treatment will not start on weekends since most staff are off work. Patients receive physical tests on D_0 and start treatment on D_1, therefore, they cannot be admitted on Friday or Saturday. However, existing treatment can be continued on weekends. To ensure that patients will stay in the same ward in each session, constraints {9} and {10} are formulated. Consequently, taking into account the chemotherapy protocols, patients should be hospitalized on specific days. Take $k=1$ (ELF protocol of gastric cancer) for example, the set of hospitalized days of $HD\{1\}$ is {1 2 3 29 30 31 57 58 59 85 86 87 113 114 115 141 142 143}, hence constraints {11}-{14}. Constraints {15} and {16} are variable constraints.

6. Objective function

$$\text{Max} \frac{\sum_{p=1}^{|P|}\sum_{j=1}^{|J|}\sum_{t=1}^{|T|} x_{pjt} + \sum_{i=1}^{|I|}\sum_{j=1}^{|J|}\sum_{t=1}^{|T|} y_{ijt}}{\sum_{j=1}^{|J|}\sum_{t=1}^{|T|} z_{ijt}} \quad \{17\}$$

In objective function {17}, the goal is to maximize the usage of hospital beds. The denominator denotes the sum of all available beds within the scheduling period, while the numerator denotes the number of all beds occupied by patients in the same period.

Note that although bed usage is positively correlated with the number of inpatients, maximizing bed usage does not necessarily correlate with more incoming patients. We analyze this issue in the following section.

7. Properties and characteristics

According to statistics from the field, the majority of patients (>95%) can finish receiving a session of treatment, meaning that a patient's treatment course is unchangeable in a session. We consider a scenario where a small number of patients, after starting chemotherapy, must postpone/stop the planned session or change their chemotherapy protocol. In this case, we will consider them as new patients the next time they come to the hospital for chemotherapy. Consequently, their postponed or modified chemotherapy protocol can be seen as a new one. Under Assumption 5 that our scheduling period does not exceed the minimum interval between two consecutive sessions of all chemotherapy protocols, each inpatient assignment only needs to assign beds for one session to inpatients. Thus, the model can be well applied.

As in Conforti's reports [14,15], the model we created is an "application driven" combinatorial optimization model. The computation of this model grows as the scale of this problem increases: number of inpatients, number of beds and length of the scheduling period. In reality, we can prove this problem to be NP-complete (see Appendix A). However, we focus more on the process of obtaining a good solution instead of having an acceptable solution. Considering practical requirements, we do not need to solve this problem in real time. Instead, we can do it offline. Hence, we can use standard commercial solver to solve this problem.

A sample study

Preliminary numerical experiments were carried out to test and validate the performance of the proposed model. We collected the admission records from June to August in 2014 at the oncology care center of FAHOXJTU, one of the largest in northwestern China. Considering that there are various types of cancers, diverse chemotherapy protocols and complex reality, it would be unrealistic to assign inpatients solely based on historical data. Therefore, we sorted through the field data and constructed calculation examples accordingly. Eight scenarios were constructed based on our field data and their main characters are described as follows:

32 chemotherapy wards including 24 four-bed wards and 8 two-bed wards, all beds are available.

Scheduling period of one week (from Monday to Sunday, $|T|=7$)

Time horizon of 343 days (duration of longest protocol and $|T|$)

$|P|$=152 patients that have been scheduled. For each booked patient, the start day of the treatment is known (SD_p).

$|I|$=64 patients waiting to start the treatment course.

12 different common chemotherapy protocols (Table B1, Appendix B). There may be various chemotherapy protocols for one kind of cancer,

each of which leads to a pattern of bed occupancy. However it is possible that different chemotherapy protocols, despite differences in drug use, result in the same pattern of bed occupancy. We selected these 12 common chemotherapy protocols (Table B1, Appedix B) because they and their derived protocols are able to cover over 90% of all bed occupancy patterns during chemotherapy.

1. Description of eight scenarios

The eight scenarios are listed as follows:

Scenario 1: Standard scenario, the same as the model we built in Section 3.

Scenario 2: Waiting patients should start their treatment immediately $(l_i = e_i)$ .This means that Constraints {5} are changed to be $\sum_{j=1}^{|J|} z_{ije_i} \leq 1$.

Scenario 3: Waiting patients can extend their treatment delay by one day. In other words, Constraints {5} are changed to be $\sum_{t=e_i}^{\min(l_i+1,|T|)} \sum_{j=1}^{|J|} z_{ijt} \leq 1$.

Scenario 4: Waiting patients can start treatment on Saturday. In this case, Constraints {6} are changed to be $\sum_{w=1}^{|T|/7} z_{ij(7*w-1)} = 0$.

Scenario 5: Waiting patients can start treatment on weekends, which means that Constraint {6} can be dropped.

Scenario 6: Constraint {8} is deleted so that waiting patients do not have to stay in the same ward within a session.

Scenario 7: We change the objective to maximize the number of waiting patients who have started treatment. Therefore, the objective function $Max \sum_{i=1}^{|I|} \sum_{j=1}^{|J|} \sum_{t=1}^{|T|} z_{ijt}$ is used to substitute for the objective function {17}.

Scenario 8: Manual method. This is the method currently used in oncology care centers. Inpatients are assigned on a first-come, first-served basis. Waiting patients will leave or be referred to other oncology care centers if no beds are available.

2. Computational results

The hardware platform for the experiment was a PC with a Pentium B960 (2.2 GHz) processor and 4GB RAM running Windows 7 Professional. We used CPLEX 12.5 MIP solver with its default settings as the optimizer to solve the integer linear programming models of scenarios 1 to 7. Scenario 8 was implemented using MATLAB and the program was run 10,000 times. The best solution from all results was taken as the final one.

Computational results are shown in Tables 2 and 3. Table 2 lists the number of available beds for each day of the week. It can be seen from Table 2, that bed demand increases from Monday, peaks on Thursday, and drops gradually afterward. If charted, bed occupancy would be a near reversed bell-shape curve. This is because a chemotherapy session for most patients is completed within five days after initiation and no patients start a new round of treatment on weekends. Also, we assumed all beds are available at the beginning. As a result, the most free beds are on Monday. After a weekend break, many patients would arrive in the hospital on Monday. They, along with the accumulating patients during the week cause bed shortages lasting from Wednesday to Friday. However, as oncology care centers do not accept patients on weekends, the bed demand decreases on weekends. Therefore, Thursday is when the bed occupancy peaks.

Discussion of managerial implication

We first compared the MIP approach with the manual method, namely, Scenario 1 with Scenario 8. It was shown that the MIP approach is superior to the manual method. Because with manual bed assignment, patients who cannot find available beds are deleted from the set of waiting patients, this means part of the solution space is discarded. Moreover, the value in Scenario 8 is the best solution obtained after 10,000 rounds of computation. Its average value (bed occupancy being only 57% and the average number of unscheduled patients standing at 39 persons) is far from that of our MIP approach.

We next examined the effect of adjusting (shortening or extending) the patient's waiting time window on the results. Theoretically, shorter waiting time is better for patients, because early initiation of chemotherapy is good for cancer control while a delayed chemotherapy session may exacerbate the patient's health condition. Therefore, it is of great clinical significance to start chemotherapy as soon as possible for cancer patients. It can be seen from a comparison of Scenario 1 and Scenario 2 that if the waiting time window is removed, bed usage will drop by roughly 1.5%. However, the almost negligible decrease would cause an increase of unscheduled patients by nearly 90%. This implies that the removal of the waiting time window would render more patients "bedless" instead of increasing bed usage significantly. In order to study the effect of prolonged waiting time window, we built Scenario 3.

Table 1. Typical cancer protocols

Cancer type	Protocol	Total cycles	Cycle length (days)	Therapeutic measures for each cycle: Drug	Dosage	Therapy route	Therapy days	Hospitalized days per cycle
Gastric cancer	ELF	6-8	28	Etoposide	120mg/m^2	iv	D2-D4	D1-D3
				Leucovorin	200mg/m^2	iv	D2-D4	
				Fluorouracil	500mg/m^2	iv	D2-D4	
Liver cancer	CAF	6-8	21/28	Cisplatin	20mg/m^2	ivd	D2-D5	D1-D4
				Adriamycin	40mg/m^2	iv	D2	
				Fluorouracil	400mg/m^2	iv	D2-D5	
				Interferon	500,000unit/m^2	sc	D2-D5	
Pancreatic cancer	SMF	6-8	56	Streptozotocin	100mg/m^2	iv	D2;D9;D30;D37	D1;D8; D29;D36
				Fluorouracil	600mg/m^2	iv	D2;D9;D30;D37	
				Mitomycin	10mg/m^2	iv	D2	
Bladder cancer	CAP	3	21/28	Cyclophosphamide	650mg/m^2	iv	D2	D1-D2
				Adriamycin	50mg/m^2	iv	D3	
				Cisplatin	70-100mg/m^2	iv	D2	
Malignant lymphoma	MOPP	6-8	28	Chloromethamine	6mg/m^2	iv	D2	D1
				Vincristine	4mg/m^2	iv	D2	
				Methylhydrazine	100mg/m^2	po	D2-D14	
				Prednisone	40mg/m^2	po	D2-D14	

iv: intravenous, ivd: rapid iv, sc: subcutaneous, po: per os

Table 2. Number of available beds

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Scenario 1	56	36	22	0	28	47	18
Scenario 2	49	39	23	0	28	47	30
Scenario 3	55	37	21	0	28	47	17
Scenario 4	54	32	10	0	1	27	18
Scenario 5	52	32	10	0	0	2	16
Scenario 6	54	34	22	0	28	48	20
Scenario 7	56	41	25	0	31	51	19
Scenario 8	52	41	27	22	46	55	31

The comparison of Scenario 1 and 3 revealed an interesting phenomenon: the prolonged waiting time window cannot increase bed usage or greatly reduce the number of unscheduled patients. It can be inferred that the time window affects bed usage only when its value is set within a specific range. Outside that effective range, its impact on bed usage becomes insignificant. Therefore, extending the patient's waiting time does not help in either clinical treatment or bed shortages. It can be concluded from the comparison of Scenario 2 and 3, that oncology care centers should give chemotherapy to patients as soon as possible because it not only benefits patients but also helps to maintain high bed usage.

In China, most oncology care centers are closed on weekends so that doctors can rest. However, for cancer patients, this may cause a delay of their treatment. In order to measure this effect quantitatively, we designed Scenarios 4 and 5. We assumed that if the oncology care center is open on Saturday, then bed usage will increase. This conjecture was corroborated by the computational results. The results showed that if the oncology care center was open on Saturday, then bed usage would grow by as much as 8.6%, the number of unscheduled patients would be reduced by 13 persons, and the high bed occupancy would last until Friday instead of Thursday. However, when we compared Scenarios 4 and 5, we found that the bed usage in Scenario 5 was only 4% higher than in Scenario 4. The reason is that all existing patients arrived on weekdays for treatment. Ultimately, if patients know that the hospital is also open on weekends, admission would change so that bed demand will be smoothed throughout the week. Considering patient preference in arrival,

Table 3. Computational results

Scenario	*Bed occupancy* %	*Number of unscheduled waiting patients*	*Computational time (seconds)*
Scenario 1	71.84	13	49084.25
Scenario 2	70.33	24	213.87
Scenario 3	71.84	11	89665.90
Scenario 4	80.49	0	101900.73
Scenario 5	84.47	0	227306.34
Scenario 6	71.84	13	12541.94
Scenario 7	69.37	11	555.54
Scenario 8	62.66	30	200.39

computational results, and doctors, we suggest that the oncology care center should be open from Monday to Saturday if possible. In this way, the waiting list can be reduced and patients can start treatment sooner. Meanwhile, bed usage can be increased to produce more economic benefit.

Normally, Constraint {9} is realistic. To patients, consecutive stays in the same bed is good for their comfort and clinical management. However, in extreme cases, some patients strongly demand to be admitted even if they must change beds frequently. That is why we designed Scenario 6. Surprisingly, we found from the comparison of Scenarios 1 and 6, that the computational results remained largely the same with or without Constraint {9}. This means the MIP approach is highly efficient and there would be not much room for improvement even if Constraint {9} is removed. For this reason, oncology care centers should consider using Constraint {9} when assigning beds to patients as it provides both convenience and efficiency.

When designing the objective function {17}, we aimed to facilitate the efficient use of medical resources, therefore we selected the maximum bed usage. As for patients, however, they wish to start chemotherapy as soon as possible. The objective function should therefore seek to maximize the number of patients starting to receive treatment. The two objective functions are positively correlated but not completely the same. To verify their difference, we designed Scenario 7. From the comparison of Scenarios 1 and 7, we noticed only a minor difference in data between them. With the solution results, we found that if the maximum admission was used as the objective function, then it was difficult for certain patients needing a long period of hospitalization to be selected. Therefore, the objective function {17} is more suitable for our model.

Conclusion

This paper addressed the problem of scheduling chemotherapy receiving inpatients, which has not been considered in previous published work. The problem concerns chemotherapy protocols of inpatients and a set of clinical constraints. These parameters greatly complicated the problem. We constructed a mathematical model of this problem and proved it to be NP-complete. As the problem solving did not require much instantaneity, we used CPLEX to solve this model and simulated the oncology care center's manual scheduling method through programming. Computational results showed that our MIP approach outperformed the manual scheduling method in reducing waiting times, allowing more admissions, and increasing bed usage. Furthermore, after constructing and solving the other seven scenarios, we analyzed and compared the results. We summarized a few laws from them to provide some recommendations for the management of oncology care centers.

Future work should focus on two issues. First, a very natural extension is inpatient assignment and can be combined with physicians' schedule to balance their workload. Second, some patients receive both chemotherapy and radiotherapy, and an integrated optimization can be taken into account.

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Conflict of interests

The authors declare no confict of interests.

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Appendix A

Theorem 1. The chemo-receiving inpatients' assignment problem is NP-complete.

Proof of Theorem 1. The proof is done by reducing polynomially the Multiprocessor scheduling problem to a special case of our bed assignment problem. The Multiprocessor scheduling problem can be defined as follows: give a set $\boldsymbol{T}$ of tasks, number $\boldsymbol{m} \in \boldsymbol{Z}^{+}$ of processors, length $\boldsymbol{l(t)} \in \boldsymbol{Z}^{+}$ for each $\boldsymbol{t} \in \boldsymbol{T}$, and a deadline $\boldsymbol{D} \in \boldsymbol{Z}^{+}$, is there a $\boldsymbol{m}$-processor schedule for $\boldsymbol{T}$ that meets the overall deadline $\boldsymbol{D}$, i.e. a function $\boldsymbol{\sigma}: \boldsymbol{T} \to \boldsymbol{Z}_{0}^{+}$ such that, for all $\boldsymbol{u} \geq \boldsymbol{0}$, the number of tasks $\boldsymbol{t} \in \boldsymbol{T}$ for which $\boldsymbol{\sigma(t)} \leq \boldsymbol{u} < \boldsymbol{\sigma(t)} + \boldsymbol{l(t)}$ is no more than $\boldsymbol{m}$ and such that, for all $\boldsymbol{t} \in \boldsymbol{T}$, $\boldsymbol{\sigma(t)} + \boldsymbol{l(t)} \leq \boldsymbol{D}$? The Multiprocessor scheduling problem is known to be NP-complete [23].

For each instance of Multiprocessor scheduling problem, we transform it polynomially into an instance of our inpatient assignment problem defined as follows: there are $\boldsymbol{|T|}$ inpatients, suppose their chemotherapy has only one cycle, patient's length of chemotherapy **is** $\boldsymbol{l(t)}$, oncology care center has number $\boldsymbol{m} \in \boldsymbol{Z}^{+}$ of beds, the deadline of inpatient assignment is $\boldsymbol{D}$. The question is whether there is a medical plan that maximizes bed occupancy, i.e. there is a maximal $\frac{\sum_{t \in T} l(t)}{D * M}$.

If Multiprocessor scheduling instance has a solution, then for all $\boldsymbol{u} \geq \boldsymbol{0}$ the number of tasks $\boldsymbol{t} \in \boldsymbol{T}$ for which $\sigma(t) \leq u < \sigma(t) + l(t)$ is no more than m and such that, for all $t \in T$, $\sigma(t) + l(t) \leq D$. This leads all inpatients having beds and complete chemotherapy within specific days and there exist a maximal $\frac{\sum_{t \in T} l(t)}{D*M}$. The reverse is also true. Hence, each Multiprocessor scheduling instance has a solution if and only if its corresponding inpatient assignment problem has a solution. Together with the NP-completeness of the Multiprocessor scheduling problem concludes the proof.

Appendix B

Table B1. Chemotherapy protocols used in this article

No	*Type of cancer*	*System involved*	*Protocol*
1	gastric cancer	gastrointestinal	ELF
2	liver cancer		CAFI
3	pancreatic cancer		SMF
4	esophagical cancer		EDF
5	gallbladder cancer		FLP
6	colorectal cancer		HDLF
7	bladder cancer	urogenital	CAP, MVAC
8	testicular cancer		EF
9	kidney cancer		IIF
10	prostatic cancer		CFP
11	acute myeloid leukemia	hematological	DA
12	malignant lymphoma		MOPP