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A multi-appointment patient scheduling system with machine learning and optimization

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ABSTRACT

Appointment scheduling is critical to increasing resource utilization and operational performance in various industry domains, especially healthcare. Costs to care for several serious diseases are projected to grow due to the aging population and rising drug prices. Thus, there is an urgent need for efficient operational planning and scheduling to reduce expenses. This research explores ways to effectively schedule outpatient chemotherapy visits with multiple appointments requiring different resources. The study aims to assess the impact of patient no-shows and individual stochastic appointment durations in scheduling performance and determine if overbooking is viable to mitigate the adverse effects of patient no-shows. The study first applies artificial neural networks (ANN) to calculate patient no-show probabilities and individualized appointment durations. Then, it builds several optimization models that use the ANN models' outcomes to schedule outpatient chemotherapy visits. The performance of patient schedules obtained from these optimization models is assessed using simulation analysis to identify the effectiveness of overbooking to combat patient no-shows and determine if individual stochastic appointment durations produce better key performance indicators.

1. Introduction

The total annual cost of cancer care in the US is estimated at 143.7 billion dollars [1]. Because the number of cancer incidents is projected to grow by 30% from 2010 to 2030, healthcare providers, researchers, and policymakers have been investigating ways to provide quality and cost-effective treatments to cancer patients [2,3]. Due to the increasing cost of cancer care, clinics that provide outpatient cancer care, such as chemotherapy treatment, are under pressure to stay cost-effective, increase resource utilization, and maintain high-quality care. These centers explore ways to effectively schedule outpatient chemotherapy visits to reduce patient congestion and long waiting times averaging over 100 min, causing patient dissatisfaction and decreasing the morale of healthcare providers [4]. Outpatient chemotherapy scheduling is considered an application area within outpatient scheduling in which appointment times and resources are assigned to patients who seek non-emergency medical attention.

One of the primary challenges in outpatient chemotherapy scheduling is to account for various clinical pathways characterized by a sequence of appointments, each of which uses different resources and has different appointment durations. Patients, based on their conditions and treatment plans, go through various combinations of these appointments during their visits. Thus, it is crucial to account for the coordination of multiple appointments and align patient routes with each appointment's resource capacity to avoid long waiting times, bottlenecks, and congestion. Fig. 1.a illustrates the concept of multi-appointments that patients go through during their chemotherapy visits, while Fig. 1.b exemplifies three pathways with multi-appointments requiring different durations. V_i^{α} stands for the αth appointment of visit V of patient i where $\alpha \in$ pathway P. R and T denote resources and timeslots, respectively. Patient waiting time occurs when an appointment does not start right after its predecessor.

Resource overtime occurs when resources need to work beyond regular working hours to serve the last assigned patient. Idle time occurs when resources are not assigned to patients during their regular working hours. It is critical to consider the following factors in outpatient chemotherapy scheduling. (1) Each patient visit may involve multiple appointments. (2) Appointments and resources may differ from one patient to another. (3) Some resources are shared among patients taking different pathways. (4) Appointment durations vary and can differ even for the same appointment based on particular patient needs. Another important challenge of outpatient chemotherapy scheduling is patient no-shows [5], which occur when patients do not attend their

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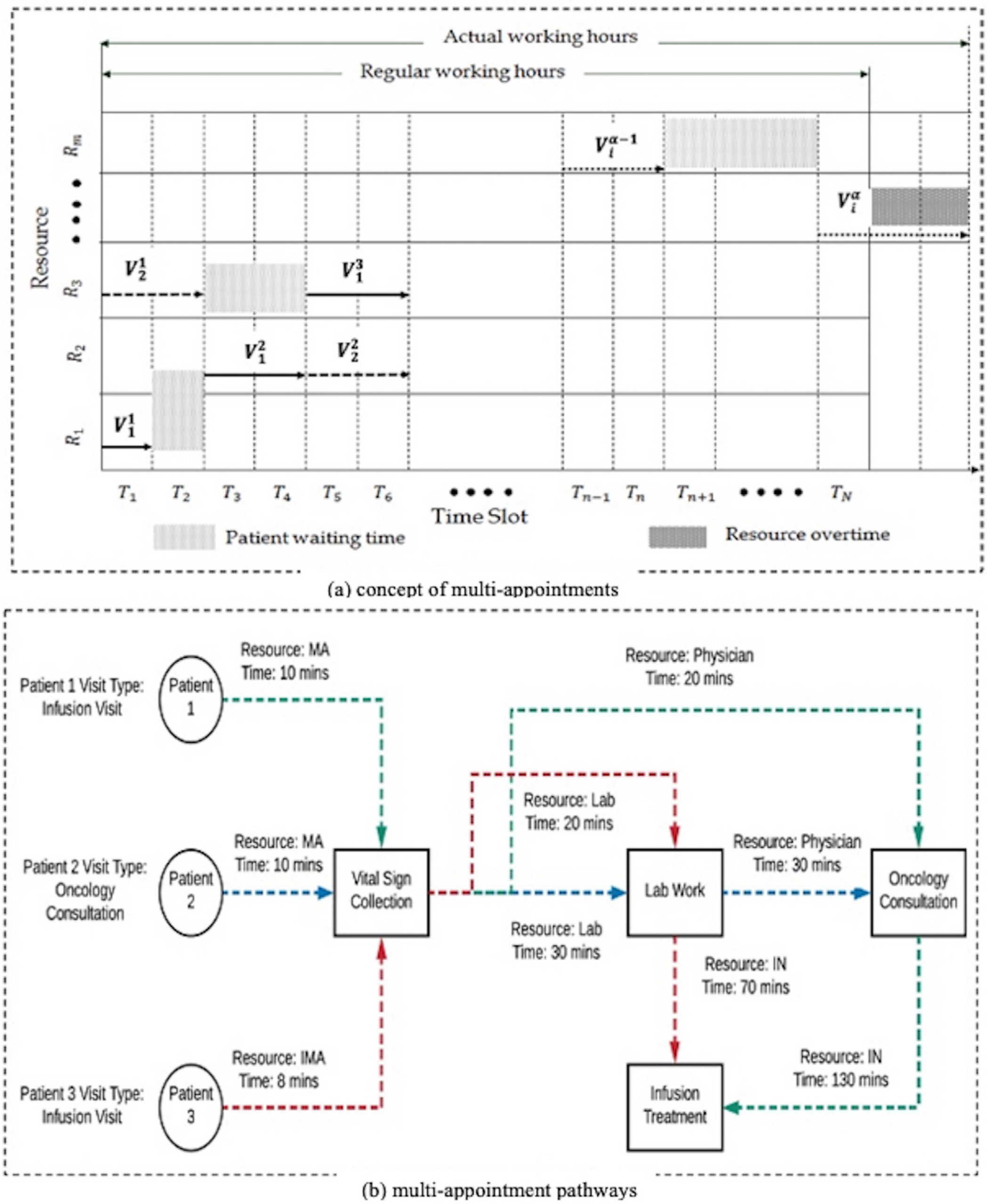

Fig. 1. Multi-appointment outpatient chemotherapy scheduling.

appointments without giving prior notice [6–8]. Patient no-shows drastically reduce resource utilization and operational efficiency, thus increasing healthcare costs. To combat patient no-shows and increase resource utilization, several researchers recommend employing an overbooking strategy in which multiple patients are scheduled for the same timeslot [9–11]. However, there is an argument stating that overbooking is difficult and can cause further congestion and be destructive to quality of care if it is implemented without using historical data and identifying patients' no-show probabilities [12]. For example, overbooking two patients with low no-show rates can cause further congestion and increase waiting time because it is likely that both patients will show up for their appointments. Thus, there is a need to determine patients' no-show probabilities based on data before overbooking them.

Another obstacle that practitioners face while developing effective outpatient scheduling tools is the highly variable appointment durations. Several studies propose to use probability distributions, instead of deterministic durations, to account for this variability and design more realistic schedules [13]. However, using a probability distribution to determine appointment durations does not account for the variability that depends on patients' characteristics, such as their age, gender, previous visits. For example, applying a probability distribution for infusion therapy appointment durations would not necessarily assign longer durations to patients who have had complications during their previous infusion therapy appointments. Thus, capturing the variability in appointment durations by estimating individual durations that are much more granular than using probability distributions may improve scheduling performance.

To this extent, this research aims to develop a method that can schedule outpatient chemotherapy visits by considering clinical pathways with multi-appointments, patient no-show probabilities, overbooking, and individual stochastic appointment durations. Although the research focuses on outpatient chemotherapy scheduling, this study and its results can also be generalized to any outpatient scheduling application. This research applies machine learning to historical data with individual patient characteristics to compute the no-show probabilities and appointment durations of patients. This scheduling method accounts for most of the variability in the clinic and generates implementable and realistic patient schedules.

The remainder of this paper is organized as follows. First, relevant articles regarding outpatient scheduling are reviewed. Then, the research framework and methodologies are explained. Afterward, the results obtained from the models are provided, and the primary findings of this study are discussed. Finally, several recommendations regarding outpatient chemotherapy scheduling are offered to future researchers and healthcare practitioners.

2. Literature review

The majority of outpatient scheduling studies focus on one clinical pathway with a single appointment either using rule-based heuristics and simulation [14–16], integer programming, metaheuristics, and simulation [9–11,17], or stochastic programming [18–22]. For example, Berg et al. [18] formulate a model to optimally assign patients to a single stochastic server by utilizing two-stage stochastic programming. Their model considers patient no-shows and aims to optimize an objective function that combines resource overtime, resource idle time, and patient waiting time. Similarly, Erdogan and Denton [19] use two-stage stochastic optimization to find the optimal arrival times of patients visiting a single server with random service durations. However, these research studies do not consider multiple appointments and various clinical pathways.

Most outpatient clinics treat patients with various requirements, and these patients go through different sequences of appointments during their visits. Thus, several studies consider multi-appointments to incorporate real-world constraints and complex patient flows and apply integer programming and heuristics to solve them [23–27]. For example, Lin [27] utilizes the mixed integer programming approach and considers multiple appointments by allowing patients to go through a sequence of procedures, each of which necessitates deterministic clinical resources and service durations. Similarly, Azadeh et al. [23] use mixed integer programming and formulate an online patient scheduling problem with multiple appointments at a pathology laboratory. However, these studies do not address random service durations and patient-no-show.

In most of the outpatient scheduling studies, appointment durations are assumed to be deterministic and known in advance [9,10,23,25]. Since it is established that appointment durations are stochastic, several papers incorporate uncertain appointment durations using probability distributions in the simulation stage of their models [15,26]. Although considering stochastic appointment durations in the optimization stage allows that the random nature of the problem is preemptively reflected in the solution, providing better and more robust results, few studies use stochastic appointment durations in the optimization stage [13,21,28,29]. The research conducted by [30] offers a methodology predicting an appointment duration using ML algorithms. However, this paper does not incorporate multi-step appointments and patient-shows. Although the literature is rich in predicting patient no-shows and preventing it with various intervention techniques using ML [31,32], very few studies use patient no-show probabilities in appointment scheduling. While it is common for many papers to assume that patients show up for their appointments [33–36], there is evidence that this assumption is mostly unwarranted. To address this gap in the literature, few studies consider no-shows [14–16,34], and overbooking [9–11,37]. For example, Liu and Ziya [11] research how capacity-related decisions should be made when taking patient no-shows into account. Their research focuses on outpatient scheduling with a single appointment, utilizes both deterministic and exponentially distributed service durations, and builds two models using queuing theory.

Based on this literature review, we observe that many outpatient scheduling papers assume clinical pathways with one appointment [17,33,35,38–40]. Studies considering multiple appointments [25] assume that all patients follow the same pathway. Among the papers considering patient no-shows, few employ an overbooking strategy [9,11]. Additionally, most of these studies use probability distribution functions to compute no-show probabilities, instead of using machine learning to estimate individualized patient no-show probabilities based on historical data. Similarly, studies that formulate the scheduling problem using stochastic appointment durations use a probability distribution and do not build machine learning models to compute individualized appointment durations based on factors, such as patients' medical history.

This research makes its primary contribution to the literature by considering multi-pathways with multi-appointments and concurrently incorporating no-shows, overbooking, and individual stochastic appointment durations when scheduling outpatient chemotherapy visits. To the best of our knowledge, this is the first study simultaneously addressing all these elements in outpatient scheduling, particularly in outpatient chemotherapy scheduling. Additionally, no-show probabilities and individual stochastic appointment durations are computed through a machine algorithm called artificial neural networks (ANN). Instead of employing homogenous probability distributions that limit applicability and generalizability, using patient characteristics to compute patient no-show probabilities and capture stochasticity in appointment durations via ANN is also a new contribution to the literature.

3. Methodology

Our multi-phase research methodology is depicted in Fig. 2. In the first phase, we develop several ANN models to estimate patient no-show probabilities and appointment durations using a historical dataset. The patient no-show ANN model – called ANN_{PNS} hereafter, where *PNS* refers to patient no show – is utilized to predict the patient no-show probabilities used in the optimization stage and identify the primary factors contributing to patient no-shows. The appointment duration ANN models – hereafter called ANN_{α}, where α refers to the appointment type – are deployed to predict the individual stochastic appointment durations used in the optimization stage.

The second phase develops four deterministic optimization models, namely DET, NSOB, SAD, and SADNSOB, to schedule outpatient chemotherapy visits. DET is a deterministic outpatient chemotherapy scheduling model and provides a baseline to analyze the impact of patient no-shows, overbooking, and individual stochastic appointment durations. DET also offers a solid modeling foundation to incorporate uncertainty and create the remaining three optimization models. SAD deploys the ANN_{α} models to account for individual stochastic appointment durations and assesses if using individual stochastic appointment durations while scheduling patients enhances KPIs. NSOB applies the individual patient no-show probabilities acquired from the ANN_{PNS} model and evaluates if the overbooking strategy to combat patient no-shows is effective or detrimental to KPIs. SADNSOB applies both the ANN_{PNS} and ANN_{α} models with the overbooking strategy to account for patient no-shows and individual stochastic appointment durations. SADNSOB aims to determine how incorporating patient no-shows, individual stochastic appointment durations, and overbooking when scheduling patients impact KPIs. It is important to note that SAD and SADNSOB are also deterministic models that incorporate the randomness in the appointment durations through the ANN models. The optimization models developed in the second phase are difficult to solve using methods that guarantee optimality in a reasonable amount of time. Thus, a heuristic approach based on genetic algorithms (GA) is constructed in the third phase to solve them.

3.1. Artificial neural network models

ML has been increasingly used in the healthcare field to improve treatment outcomes, enhance healthcare quality, and reduce healthcare

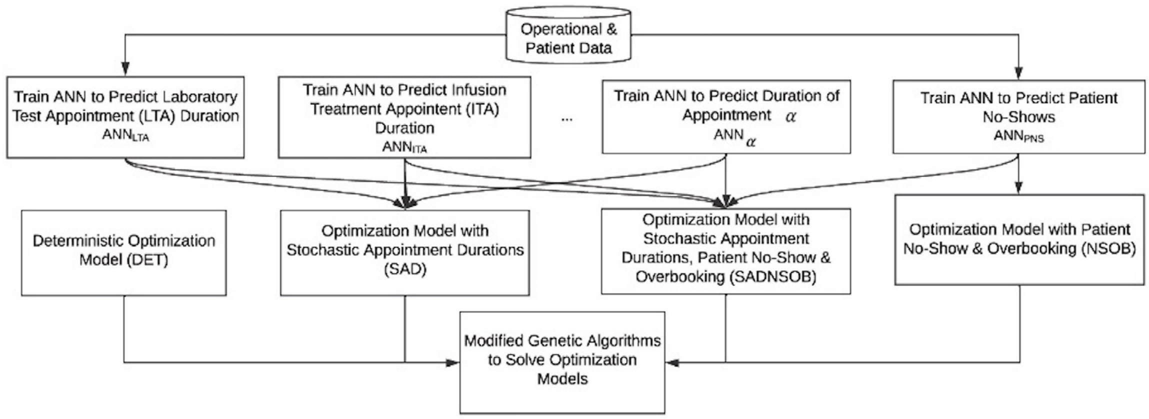

Fig. 2. Research methodology.

costs [41–47]. We apply the Artificial Neural Network (ANN) algorithm and create the ANN_{α} models to predict the individual stochastic appointment durations. For each appointment type α, an ANN model with a single hidden layer is built. For the hidden layer, a rectified linear activation function (ReLU) is used. ReLU is a nonlinear function that enables the ANN structure to model nonlinear relationships. Because ReLU sets the negative values to zero, it results in much fewer activations, reducing the computation time drastically [48]. Since the appointment durations used in the optimization models are discrete and represented as timeslots, the output activation function that rounds the predicted target variable to the nearest integer is selected, as depicted in Eq. (1). This allows continuous predicted values to be converted to discrete timeslots.

$$g(\beta) = \lceil \lfloor 2\beta \rfloor /2 \rceil \text{, } where\ \beta = g(\sum_{p=1}^{P} w_{p1}^{\mathrm{h}} a_p + b) \tag{1}$$

We apply the ANN algorithm and create the ANN_{PNS} model to predict the patient no-show probabilities. The target variable of the ANN_{PNS} has two categories – "Yes" and "No" – encoded using 1 and 0, respectively. 1 indicates scheduled patient visits for which the patient did not show up, while 0 represents the visits that patients attended. For the hidden layer, the ReLU activation function is applied because it reduces the computational time and still models the nonlinear relationships among the input and target variables. A sigmoid function for the activation function in the output layer is used to convert the predicted target variables into probabilities that range between 0 and 1. The output of this activation function given in Eq. (2) indicates the probability of patients not showing up for their appointments.

$$g(\beta) = 1/(1+e^{-\beta}), where\ \beta = g(\sum_{p=1}^{P} w_{p1}^{\mathrm{h}} a_p + b) \tag{2}$$

3.2. Optimization models

We provide the mathematical formulations of the four optimization models with different assumptions regarding patient no-shows, overbooking, and individual stochastic appointment durations. DET is a deterministic model that is used as a baseline and has the following assumptions. (1) The set of patients who need to be scheduled are already known. This is a realistic assumption because the treatment plans for cancer are based on protocols and known prior. (2) The daily staffing schedule is known in advance and starts punctually. These models do not design a roster schedule of doctors and nurses; hence, the staffing schedule for a certain day is assumed to be available. (3) Daily working hours are divided into timeslots of equal length. (4) Overtime is allowed for staff. (5) All steps in an appointment need to happen in a defined sequence that cannot be altered. These steps are non-preemptible, meaning once started, they run to completion. (6) Patients are assumed to arrive punctually. (7) Patients are assumed to show up for their visits. (8) Overbooking is not allowed. (9) Appointment durations are deterministic and represented using timeslots (see Fig. 3).

The second optimization model NSOB removes the 7th and 8th assumptions of DET, considering patient no-shows and allowing overbooking. The third optimization model SAD eliminates the 9th assumption of DET and applies individual stochastic appointment durations for each appointment α in visit V of patient $I-V_i^{\alpha}$. The fourth optimization model SADNSOB removes the 7th, 8th, and 9th assumptions of DET and simultaneously considers patient no-shows, overbooking, and individual stochastic appointment durations. Table 1 provides the notation of the optimization models.

3.3. DET model

Because the SAD, NSOB, SADNSOB models are easily formulated by applying minor modifications to the DET model, we will first elaborate on the DET model and then briefly explain how to develop the remaining three models.

DET model objective function

$$Z_1 = \sum_{i \in I} \vartheta_i \tag{3a}$$

$$Z_2 = \sum_{i \in I} \sum_{\alpha \in A_p} S_{i\alpha j} - C_{i(\alpha-1)j} \tag{3b}$$

$$Z_3 = \sum_{j \in J_r} O_j \tag{3c}$$

$$Z_4 = \sum_{j \in J_r} \lambda_j \tag{3d}$$

$$Min\ Z = \sum_{x=1}^{4} w_x Z_x \tag{3e}$$

Subject to:

Appointment assignment

$$\sum_{i \in I} \sum_{\substack{\alpha \in A_p: \\ r = r_{\alpha p}}} X_{i\alpha jt} \leq 1, \forall j \in J_r, t = H_j^s, \ldots, |T| \tag{4}$$

$$\sum_{t \in T} X_{i\alpha jt} + \vartheta_i = 1, \forall i \in I, \alpha \in A_p, p \in P, r \in r_{\alpha p}, j \in J_r \tag{5}$$

Precedence Relationship

$$C_{i\alpha j} \geq S_{i\alpha j} + T_{i\alpha} - M\left(1 - X_{i\alpha jt}\right), \forall i \in I, \alpha \in A_p, p \in P, r \in r_{\alpha p}, j \in J_r, t = H_j^s \ldots, |T| \tag{6}$$

$$C_{i(\alpha-1)j} \leq S_{i\alpha j}, \forall i \in I, \alpha \backslash \{1\} \in A_p, p \in P, r \in r_{\alpha p}, j \in J_r \tag{7}$$

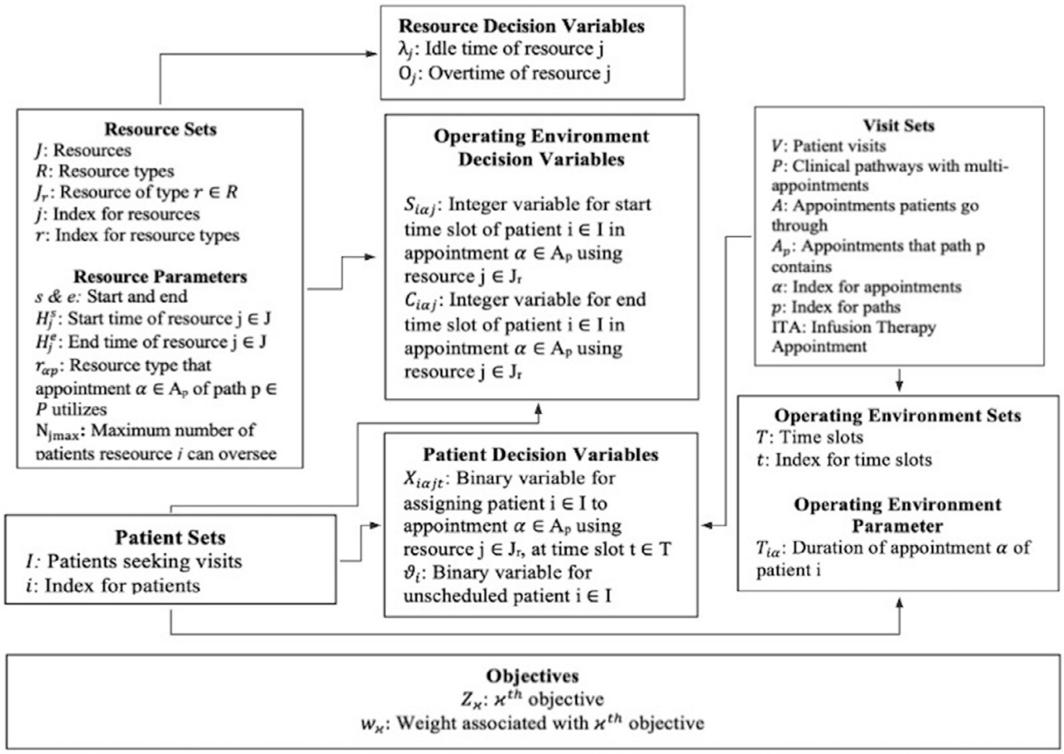

Fig. 3. Notations of optimization models.

Resource Limitations

$$\sum_{\substack{j\in J_r:\\ r=r_{\alpha p}}} \sum_{t=H_j^s}^{T} X_{i\alpha jt} \le 1, \forall i\in I, \alpha\in A_p, p\in P \tag{8}$$

$$\sum_{i\in I}\sum_{\substack{\alpha\in A_p:\\ r=r_{\alpha p}}}\sum_{t=max(t-T_{i\alpha}+1,1)}^{min(T-T_{i\alpha}+1,t)} X_{i\alpha jt}\le N_{jmax}, \forall j\in J_r, t=H_j^s\dots,|T| \tag{9}$$

Overtime and idle time

$$O_j \ge X_{i\alpha jt}(t+T_{i\alpha}-1) - H_j^e, \forall i \in I, \alpha\in A_p, p\in P, r\in r_{\alpha p} j\in J_r, t=H_j^s,\dots,|T| \tag{10}$$

$$\lambda_j = \left(H_j^e - H_j^s\right) - \sum_i \sum_{\substack{\alpha\in A_p:\\ r=r_{\alpha p}}} \sum_{t\in T} (X_{i\alpha jt}T_{i\alpha}/N_{jmax}), \forall j\in J_r \tag{11}$$

Integrality

$$X_{i\alpha jt} \in \{0,1\}, \forall i\in I, \alpha\in A_p, p\in P, r\in r_{\alpha p}, j\in J_r, t=H_j^s\dots,|T| \tag{12a}$$

$$S_{i\alpha j}\in T, \forall i\in I, \alpha\in A_p, p\in P, r\in r_{\alpha p}, j\in J_r \tag{12b}$$

$$C_{i\alpha j}\in T, \forall i\in I, \alpha\in A_p, p\in P, r\in r_{\alpha p}, j\in J_r \tag{12c}$$

$$\vartheta_i\in\{0,1\}, \forall i\in I \tag{12d}$$

The four objectives of DET are defined in Eqs. (3a) through (3d). Because chemotherapy is given in cycles, the number of chemotherapy patients to be scheduled for a given day is known. However, it is not always possible for healthcare clinics to schedule all of these patients. Thus, Eq. (3a) minimizes the number of unscheduled patients ϑ_i and ensures that timely access to chemotherapy treatment will be maximized. Eq. (3b) minimizes the sum of patients' waiting time between their two subsequent appointments α and $\alpha-1$. Equations (3c) and (3d) minimizes the resource overtime and idle time. Since most outpatient scheduling papers use a weighted combination of multiple objectives [10,13,16], we apply the same strategy and convert the optimization problem into a scaler form with one objective function by linearly combining Equations (3a) through (3d) using a set of weights.

$X_{i\alpha jt}$ is a binary variable that assigns patient i to start appointment α at time slot t to use resource j. Index j is an element of J_r, where r is the resource type of appointment α of path p. In other words, α and p determine the resource type $r\in R$, such as a registered nurse (RN) or medical doctor (MD). For example, when clinical pathway p = *1* and appointment α = medical doctor consultation appointment (MDCA), then the resource type is "r_{1MDCA}: Medical Doctor", making J_r a set of medical doctors. Thus, Eq. (4) specifies that resource j starts to execute at most one single appointment α at given time t, guaranteeing that resources will not start treating multiple patients at the same time. Patients' multiple appointments must be all scheduled during their visits; thus, Eq. (5) guarantees that either all or none of the appointments in patients' pathways are scheduled for a given day. When patient i is not scheduled for a given day, then ϑ_i will be one, forcing all $X_{i\alpha jt}$ variables of patient i to zero. Eq. (6) is a derived expression to obtain the end-time slot for each appointment $C_{i\alpha j}$ by adding the appointment duration $T_{i\alpha}$ to the start-time of appointment α $S_{i\alpha j}$. Eq. (6) ensures that the difference between the end and start timeslots of each appointment will be sufficient to cover the duration needed by that particular appointment. Eq. (7) defines the precedence constraints between two subsequent appointments and ensures that the patient's next appointment will not start until his/her previous appointment is finished. This equation also helps derive the end time of patient $i\in I$ for appointment $\alpha-1\in A_p$ using resource $j\in$ of J_r. Eq. (8) ensures that patient i is assigned to at most one resource in appointment α. Eq. (9) places an upper bound N_{jmax} to the number of patients assigned to a resource j. N_{jmax} values are set to 1 for MDs and LABs. RNs can monitor multiple patients during infusion therapy appointments (ITAs); however, there are limitations restricting the number of patients that RNs can oversee at a given time. Thus, $N_{\alpha max}$ is set to greater than 1 for RNs. Eq. (10) derives the overtime for a resource as the difference between the treatment completion time of the last patient assigned to the resource and the end of regular working hours for that resource. Eq. (11) computes the idle time λ_j of resource j by subtracting the summation of timeslots that resource j is assigned to a patient from the total timeslots that resource j is working during regular working hours. Equations (12a) through (12d) are integrality constraints and define the scope of the decision variables.

3.4. NSOB model

We formulate the NSOB model by changing Equation (4) of the DET model. First, ζ_i indicating the no-show probability of patient i is computed using the ANN_{PNS} model. Then, Eq. (4) of the DET model is modified as given in Eq. (13) to allow overbooking. As observed from Eq. (13), patients with high no-show probabilities can be overbooked together to use the same resource r of type j at the same time slot t. Eq. (13) overbooks patients only if the summation of their no-show probabilities is less than or equal to 1 to prevent resources from overloading. For example, Eq. (13) does not assign two patents with no-show probabilities of 0.4 and 0.5 to use resource j of type r at the time slot t since $(1 - .4) + (1 - .5) = 1.1 \nleq 1$. Thus, this overbooking strategy is not random and driven by patient no-show probabilities. It is important to note that this is the only modification made to the DET model to retrieve the NSOB model.

$$\sum_{i\in I} \sum_{\substack{\alpha\in A_p: \\ r=r_{\alpha p}}} (1-\zeta_i)X_{i\alpha jt} \leq 1, \forall j \in J_r, t = H_j^s \dots, T \tag{13}$$

3.5. SAD model

The SAD model is formulated by modifying several equations of the DET model. First, appointment durations $T_{i\alpha}$ are computed using the ANN_α models. For example, if α is a laboratory test appointment (LTA), the ANN_{LTA} model is used to predict the LTA duration for patient i. Then, these computed appointment durations $T_{i\alpha}$ are plugged in Eqs. (6), (9), and (10) of the DET model formulation. It is important to note that all other elements of DET remain unchanged.

3.6. SADNSOB model

The modifications adopted to obtain the SAD and NSOB models are employed simultaneously to formulate the SADNSOB model. In other words, the ANN_α models compute the duration $T_{i\alpha}$ of appointment α of each patient i. Then, the ANN_{PNS} is applied to calculate the no-show probability of each patient i. Finally, Eqs. (6), (9), and (10) of the DET model are modified using the predicted appointment durations $T_{i\alpha}$, and Eq. (4) is of the DET model is replaced by Eq. (13). All other elements of DET remain the same.

3.7. Modified genetic algorithms

We use genetic algorithms (GA) to obtain satisfactory solutions for the DET, NSOB, SAD, and SADNSOB models. GA is a heuristic optimization method based on natural selection and genetics. GA uses a population of candidate solutions and assesses the quality of potential solutions via an objective function, also known as a fitness function. The characteristics of good solutions with better fitness values are carried out iteratively to find the optimal or a near-optimal solution.

The modified GA has several components, including solution representation, crossover, mutation, and decoding procedure. Each candidate solution is represented using an array with as many elements as the number of patients expecting to be scheduled for a given day. In the GA terminology, these candidate solution arrays, and their elements are called a chromosome and genes. Each gene within a chromosome represents a patient with index $i \in I$. The location of the gene with index i in a chromosome indicates the scheduling order of patient i. It is important to note that the genes within a chromosome should have unique values because a patient cannot be scheduled more than once. Thus, the feasibility of each candidate solution is checked, and infeasible solutions are corrected by identifying repeated values and replacing them with missing ones. Fig. 4 illustrates the solution representation where the number of patients seeking visits $|I| = 5$.

Crossover is the primary process that improves candidate solutions iteratively towards the optimal solution. The crossover operator exploits the problem search space by preserving the genes within a chromosome that are responsible for desired fitness values. The crossover operator used in the Modified GA is called two-point crossover in which two points from the chosen chromosomes (i.e., parents) are randomly picked, and the genes between the two points are swapped between the parents. After crossover, the newly created chromosomes (i.e., offspring) are checked for feasibility and modified, as described above, if they are not feasible (see Fig. 5).

Mutation is an operator ensuring diversity within the population and aims to explore the search space to prevent premature convergence. In the proposed algorithm, the five-point mutation is utilized because the problem sizes considered in the optimization models are large. The mutation points within a chromosome are randomly selected. Then, the values of the selected mutation points are swapped. After reproduction, newly generated chromosomes replace the ones in the preceding generation.

In each iteration of the Modified GA, individuals are selected to apply the crossover and mutation operators. In a good selection mechanism, an individual with a better fitness value is selected with a higher probability. We adopt the roulette wheel approach as the selection mechanism in our Modified GA. This approach assigns each chromosome a slice of a roulette wheel. The slice area is proportionate to the fitness function, which is the inverse of the objective function given in Eq. (3e) for that chromosome. Then, a chromosome is selected with replacement for the next generation by spinning the wheel. This chromosome is called a parent in the GA terminology. One of the essential parts of our modified GA approach is to decode a chromosome to identify daily schedules. The patients, their pathways, appointments, estimated appointment durations, and if they are scheduled are stored using a specific data structure similar to a matrix in the GA application. This matrix has extra fields, such as the resource field indicating which resource is assigned to appointment α of patient i, the time slot fields indicating when appointment α of patient i starts and ends. This patient matrix stores $I, P, A_p, T_{i\alpha}, S_{i\alpha j}, C_{i\alpha j}, and\ \vartheta_i$. The list of resources, the appointments that they can be served, the number of patients they can oversee in each timeslot t, and their working hours are represented using a separate matrix. This resource matrix stores $J, r_{\alpha p}, J_r, H_j^s, H_j^e$.

At the beginning of the decoding procedure, these matrices are initialized. Recall that each gene within a chromosome represents a patient. We start with the first gene representing the first patient, let us call it patient i, to be scheduled. The decoding procedure determines the appointment α of patient i from the patient matrix and identifies the resources J_r that can be employed for that appointment from the resource matrix. Then, the resource matrix is scanned again to decide if there are any available resources $j \in J_r$. If there is, appointment α of patient i is assigned to use resource j at time t. Upon this assignment, several fields in the patient and resource matrices are updated. For example, the resource and time slot fields for appointment α of patient i in the patient matrix are recorded, which indirectly represents $X_{i\alpha jt}$ decision variable. Additionally, the start $S_{i\alpha j}$ and end time slot fields $C_{i\alpha j}$ for appointment α of patient i in the patient matrix are recorded as t and $t+T_{i\alpha}$, respectively. The number of patients that resource j can oversee is decreased by one between the timeslots t and $t+T_{i\alpha}$ in the resource matrix, indicating the availability of resource j at time slot t. These steps are repeated for each appointment of each patient located within a chromosome. It is important to note that when there are no available resources for the future appointments of patient i, the patient is considered unscheduled. Then, the matrices are updated again to free the resources assigned for this patient's previous appointments. After

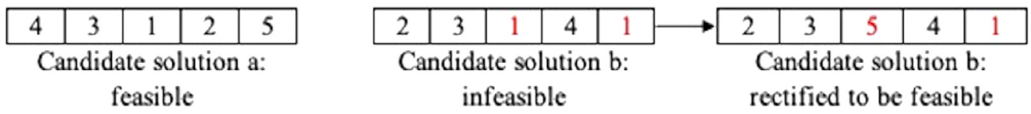

Fig. 4. Solution representation.

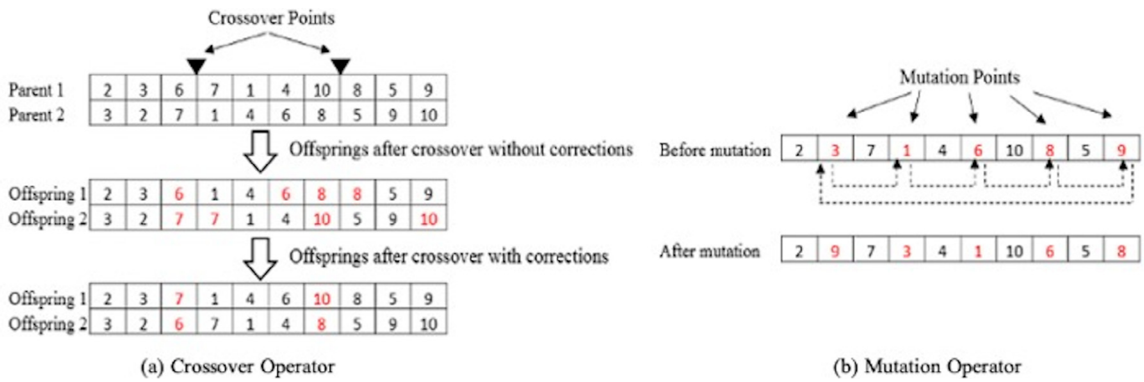

Fig. 5. Crossover and mutation operators.

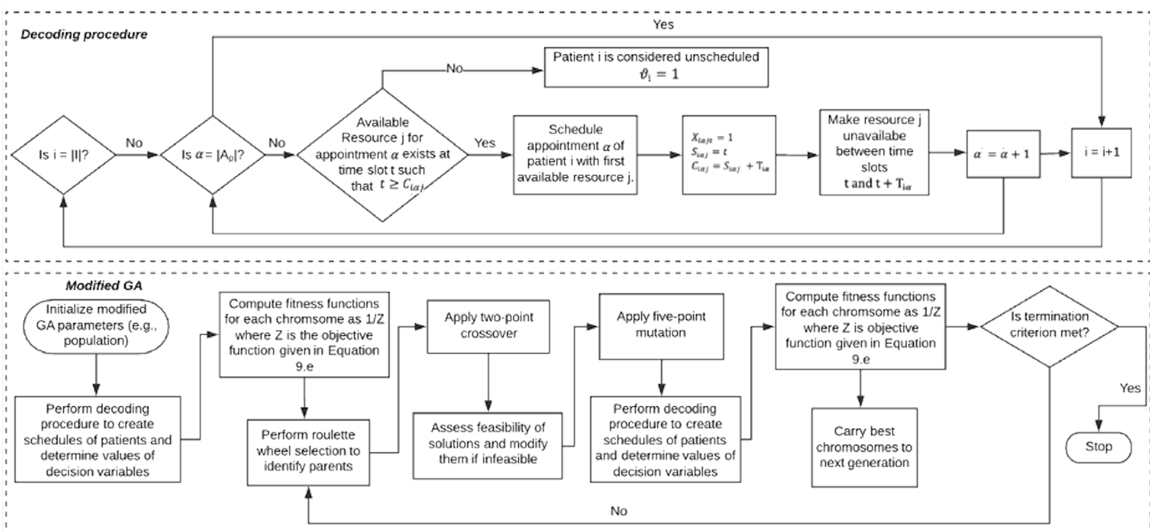

Fig. 6. Summary of modified GA.

the decoding procedure, the KPIs are computed using the patient and resource matrices and then combined via a set of weights to determine the fitness value. The summaries of the modified GA algorithm and its decoding procedure are given in Fig. 6.

4. Dataset description

The dataset used in this study 39458 visits of 2256 patients and various critical variables identified based on the domain knowledge of the clinical care team. Fig. 7 provides a brief visualization of some of these variables and indicates which variables are used in the ANN_{PNS} and/or ANN_{α} models.

The input variables in the dataset can be grouped into three categories, as shown in the first three columns of Fig. 7. The first group contains five variables, namely *"Age", "Gender", "Distance (in miles)", "Adult Household",* and *"Household Count",* and is related to patient demographics. The binary variable *"Adult Household"* indicates if an adult person lives with the patient, while *"Household Count"* stands for the number of people living with the patient. Because these variables are not readily available in the database, they are built using other fields. For example, *"Household Count"* is estimated by obtaining the number of individuals that share the same address as the patient in the database.

The second group is comprised of seven variables and is related to the treatment history of patients. It includes *"Cancer Type", "Stage", "Surgery", "Radiation", "Complications",* and regimen related variables such as *"Drugs"* and *"Drug Dose".* The variable *"Stage"* indicates how advanced cancer is and if it is local or metastasized. *"Surgery"* shows if the patient had surgery before a visit. *"Radiation"* identifies if the patient is having radiotherapy along with chemotherapy. *"Complications"* determines if the patient had a previous complication during the visit, such as pain and extravasation. *"Drugs"* and *"Drug Dose"* indicate a combination of drugs (e.g., vincristine, doxorubicin, and dexamethasone) and their doses used in an infusion therapy appointment (LTA). The visualizations for *"Drugs"* and *"Drug Dose"* variables are not provided in Fig. 7 due to high cardinality.

The third group contains eight variables and is related to patients' previous visits and appointments, such as *"Previous Visits", "Booking Window", "Reminder", "Path No",* and *"Appointment Type". "Previous Visits"* account for the number of times the patient has visited the

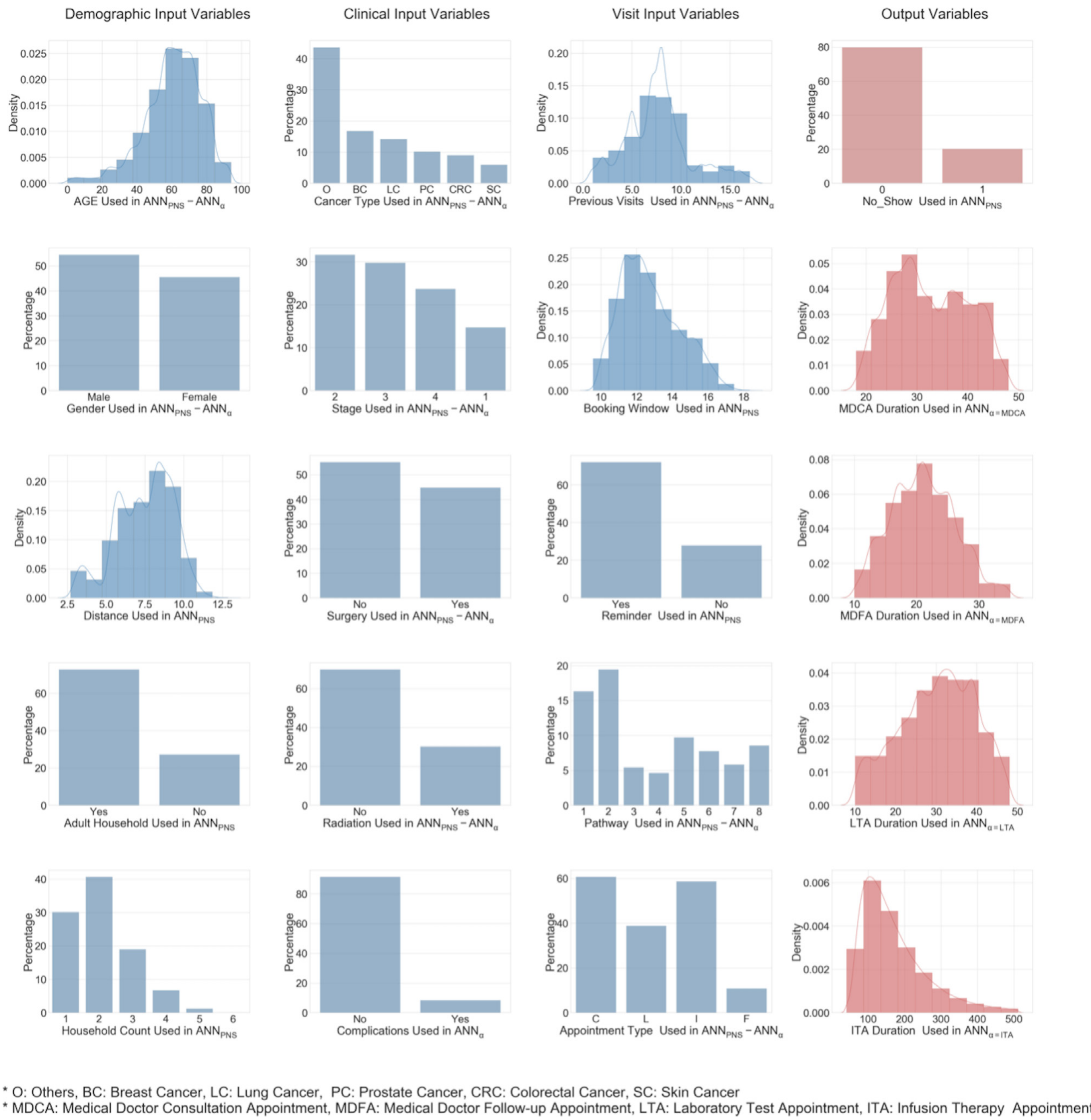

Fig. 7. Variables used in ANN_{PNS} and/or ANN_{α} models.

clinic. *"Booking Window"* indicates how many business days in advance the visit was scheduled. *"Reminder"* specifies that the clinic sent the patient a reminder and whether the patient confirmed the visit. *"Pathway"* identifies the clinical pathway indicating a sequence of appointments during the visit. *"Appointment Type"* is a set of four binary variables indicating if the patient had that particular appointment type during the visit. Using the *"Pathway"* and *"Appointment Type"* variables in the dataset, eight clinical pathways and four appointment types are identified, as given in Table 1. Recall that P denotes clinical pathways.

The dataset has five additional variables used as the output variables in the ANN_{PNS} and/or ANN_{α} models. The *"No Show"* variable is employed as the output variable of the ANN_{PNS} model. As seen from Fig. 7, 11.62% of the patient visits are considered patient no-shows.

The dataset has four appointment duration variables, namely *"MDCA Duration", "MDFA Duration", "LTA Duration", "ITA Duration".* These variables indicate how many minutes a patient's appointment of a particular type takes. Each of these output variables is used to build an ANN_{α} model for appointment type α. For example, *"ITA Duration"* is used as the output variable for the ANN_{ITA} model. The x-axes of the plots in Fig. 7 indicate if the variables are used in the $ANN_{PNS}$and/orANN_{α} models.

5. Results

5.1. Results of ANN models

When building the ANN_{PNS} model, *"Complications", "Drugs", "Drug Dose",* and a set of four appointment duration variables are excluded from the dataset because they are not identified as critical for predicting patient no-shows by the clinical staff. An ANN structure with an input, hidden, and output layers is instantiated and then

Table 1
Paths, appointments, and resource types.

Appointment type	Resource type	P1	P2	P3	P4	P5	P6	P7	P8
Medical Doctor Consultation Appointment (MDCA)	Medical Doctor (MD)	✓	✓					✓	✓
Medical Doctor Follow-up Appointment (MDFA)							✓		
Laboratory Test Appointment (LTA)	Laboratory (LAB)		✓	✓	✓				✓
Infusion Therapy Appointment (ITA)	Registered Nurse (RN)				✓	✓	✓	✓	✓

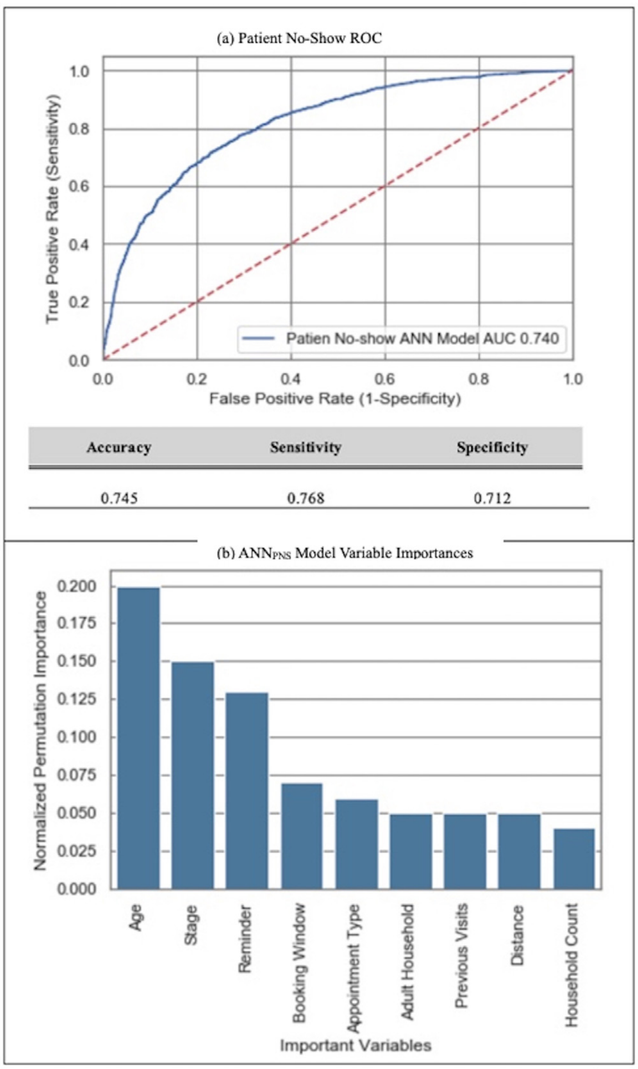

Fig. 8. ANN_{PNS} model results.

trained using the remaining 17 input variables and the *"No-Show"* output variable. 10-fold cross-validation is used in training to prevent overfitting and generate a robust model.

Fig. 8.a provides the ROC curve for the ANN_{PNS} model and reports several performance metrics, such as AUC, sensitivity, specificity, and accuracy. The patient no-show probabilities are converted to binary values using a threshold value of .5 to compute the accuracy. According to industry benchmarks, patient no-show models yield an AUC between 0.6 and 0.8 [49]. Thus, we consider that the ANN_{PNS} model performs well and can be deployed in the optimization models.

Since ANN models have a black box nature and are not easily explainable, we obtain feature importances to interpret the ANN_{PNS} model and identify the critical factors that lead to patient no-shows. The feature importances given in Fig. 8.b. indicate that *"Booking Window"* plays a critical role in identifying patient no-shows. The no-show probabilities of patients go up if patients book their visits far in advance. One way to overcome this issue is to set a deadline regarding how far future patients can book. Another way to address this issue is to send reminders closer to the scheduled visit day because the no-show probabilities of patients who received reminders and confirmed their visits are drastically lower than those who did not confirm. *"Stage"* is also an important feature that helps predict patient no-shows since the ANN_{PNS} model methodically assigns higher probabilities to patients with stage 3 and 4 cancer. This finding is critical for decision-makers and aligned with a study stating that cancer distress may lead patients to miss appointments [50].

Another critical feature determining patient no-show probability is "Age". We believe this variable is a proxy for other important features that prevent patients from showing up for their appointments. For example, older adults become increasingly transportation disadvantaged; this makes it more difficult for them to travel to the clinic. Older adults may also experience age-related impairments and decline in their cognitive and sensory functions, which may prevent them from remembering their appointment days and times.

The *"Appointment Type"* variable plays an important role in determining patient no-shows. Patients only with an LTA or MDCA have higher no-show probabilities as compared to the patients with ITA appointments. This may be because physicians educate patients regarding the importance of taking the prescribed dose of chemotherapy at the scheduled time, and patients know the adverse outcomes of missing ITA. Other important variables, such as *"Adult Household", "Age",* and *"Distance"* play a critical role in patients' mobility. For example, patients living with an adult and closer to the clinic are more likely to show up for their scheduled visits. This may be due to chemotherapy's side effects, making it difficult for patients to travel back home alone after their visits.

Twelve input variables are considered when building ANN_α models, where α is MDCA, MDFA, LTA, and ITA. The input variables used in ANN_α models include *"Drug Dose"* and *"Drugs"* in addition to the ones indicated in Fig. 7. For each ANN_α, the duration of that particular appointment type α is selected as the output variable, as shown in Fig. 7. 10-fold cross-validation is used while training to prevent overfitting and generate a robust model. Fig. 9 provides the feature importances and model performance metrics for each ANN_α model.

The ANN_{ITA} and ANN_{LTA} models yield R^2 values over 0.8, indicating that most of the variances in the ITA and LTA durations are

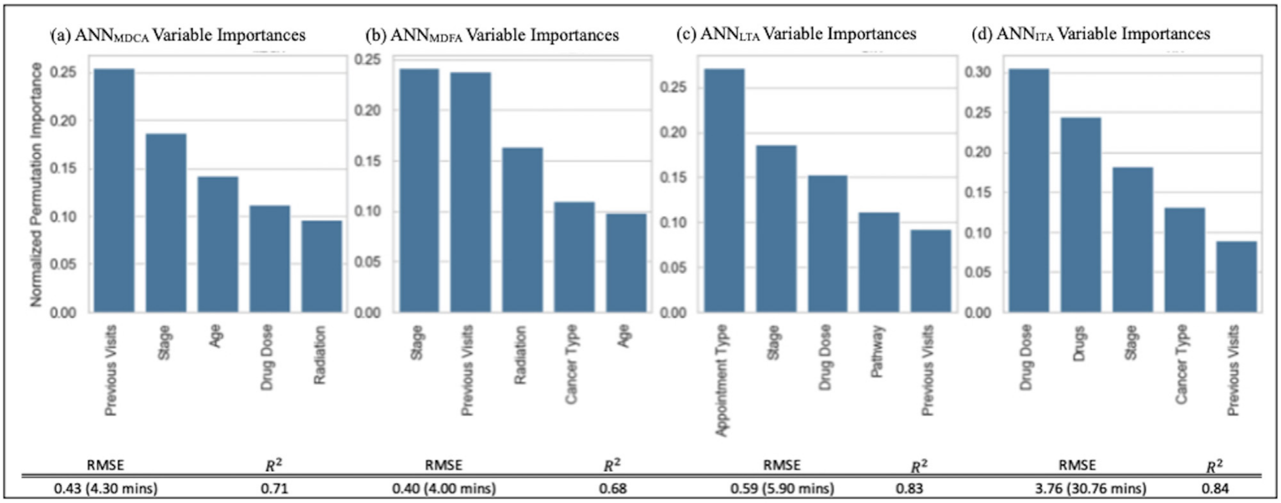

Fig. 9. Future importances and performance of ANN_α models.

explained by the input variables used in the models. The ITA appointment durations highly depend on *"Drugs"* and *"Drug Dose"* variables. This is expected as these variables together determine the rate of the drug release, thus the duration of ITAs. For example, an ITA in which a high dose drug is administrated takes longer as compared to an ITA in which the patient is given a low dose drug. LTA durations, on the other hand, mostly depend on *"Appointment Type"*. For example, the LTA durations for patients with an MDCA are predicted to be longer than the LTA durations for patients visiting the clinic for an ITA because the lab tests required before ITAs and after MDCAs are different. LTA durations also appear to be longer for patients in clinical pathways *P2* and *P3*. This indicates that the LAB may not promptly process the lab tests of these patients because their LTAs are the upstream operation and not followed by an ITA.

ANN_{MDCA} and ANN_{MDFA} give R^2 values of .71 and .68 and RMSE values of 0.43 and 0.40. *"Previous Visits"* is an important variable and inversely impacts the MDCA and MDFA durations. When patients visit the clinic more often, the MDCA and MDFA durations appear to be slightly shorter. This may be because when MDs are more familiar with their patients, they can be more efficient and discuss the treatment progress faster. *"Stage"* is also an important variable in the ANN_{MDCA} and ANN_{MDFA} models.

5.2. Results of optimization models

We first apply the DET, NSOB, SAD, SADNSOB optimization models to small problems for validation. In the small problems, the patient size $|I|$ is varied from 6 to 30, clinical pathways *P2, P4,* and *P7* and their appointments are considered, as given in Table 1, and a single resource r for each appointment type α is assumed to be available. The working hours for the clinic are 8:00 am to 05:00 pm for every resource j, which is equivalent to the start-time $H_j^s = 1$ and end-time $H_j^e = 54$ in terms of timeslots. The number of ITA patients that an RN can oversee at a given time N_{max} is set to 1. The patient demand $|I|$ for a given day is distributed to clinical pathways P proportional to their percentages in the dataset, as summarized in Fig. 7. Thus, 65%, 16%, and 19% of patients are considered to follow clinical pathways *P2, P4,* and *P7*, respectively. The deterministic durations of patients' appointments used in the DET and NSOB models are estimated using the dataset and confirmed by the clinical staff. To ensure we use accurate appointment durations, we first compute the average appointment durations using the dataset as summarized in Fig. 7 and adjust them based on the feedback obtained from the clinical staff. The average MDCA and LTA durations are 31.61 and 30.23 min and set to 3 timeslots (i.e., 30 min)

Table 2
Small problem description.

Appointment type α	Resource type r	Capacity	Deterministic duration ($T_{i\alpha}$) in timeslots & % of patients
MDCA	MD	1	3 (100% of patients)
LTA	LAB	1	3 (100% of patients)
ITA	RN	1	6 (20% of patients), 12 (25% of patients), 15 (40% of patients), 18 (15% of patients)

for all patients, while the ITA durations vary for different patient groups based on the infusion drug type and dose given, as provided in Table 2.

The patient no-show probabilities employed in the NSOB and SADNSOB models and the appointment durations utilized in the SAD and SADNSOB models are computed using the ANN_{PNS} *and* ANN_α models. Based on the input obtained from clinical staff, we identify the rankings of the weights used in the objective function. We give higher weights to the number of unscheduled patients and waiting time because access to care is critical for cancer patients. The optimization models above are formulated and then solved using the proposed GA, CPLEX IP (CIP), and CPLEX CP (CCP). When declaring the CCP model, we use interval and sequence decision variables. The interval decision variable represents a finite time duration in which a step occurs. The interval decision variable has several properties, including start time S, end time C, duration T. The interval variable can be set to become present or absent. If an interval variable is absent, all of its associated properties are set to zero. The sequence decision variable defines the sequence of appointment allocation α to each resource j. The constraints are modeled to represent the relations among all decision variables. The "span constraint" defines Eq. (5) in the DET model and is used to ensure that either all or none of the appointments during the patient's potential visit are covered. The "alternative constraint" defines Eqs. (8) and (9) in the DET model and is employed to model an exclusive alternative between allocation variables, which implies that each appointment is only allocated to one resource, and it will be executed only once. The "end before start constraint" defines Eqs. (6) and (7) and is utilized to model the sequence between the patient's appointments. The "no overlap constraint" defines Eq. (5) in the DET model and is used to model that each resource is only executing one appointment at a time. The results obtained from solving the small problems are summarized in Table 3.

There are several observations that can be made from the results obtained from the small problems, as described in Table 3. First, CPLEX

Table 3
Results of the small problem.

Model	Method	Weights	Objective function value (Z)					Computation time				
			|I|:6	|I|:12	|I| :18	|I|:24	|I|:30	|I|:6	|I|:12	|I|:18	|I|:24	|I|:30
DET	CIP	[0.04, 0.12, 0.04, 0.8]	24.9	21.0	22.0	–	–	0.2	15.7	102.4	>300	>300
		[0.04, 0.22, 0.04, 0.7]	22.5	20.2	20.5	–	–	0.2	16.8	98.5	>300	>300
		[0.1, 0.2, 0.1, 0.6]	20.8	18.1	18.3	–	–	0.2	16.5	97.1	>300	>300
		[0.14, 0.2, 0.14, 0.52]	22.1	19.3	19.9	–	–	0.2	17.5	95.7	>300	>300
		[0.14, 0.28, 0.14, 0.44]	25.6	22.1	23.3	–	–	0.2	16.4	100.2	>300	>300
	CCP	[0.04, 0.12, 0.04, 0.8]	24.9	21.0	26.1	32.4	42.9	0.2	1.5	1.5	2.4	5.4
		[0.04, 0.22, 0.04, 0.7]	22.5	20.2	24.1	29.6	40.0	0.2	1.4	1.6	2.2	5.1
		[0.1, 0.2, 0.1, 0.6]	20.8	18.1	22.1	27.6	37.0	0.2	1.4	1.6	2.2	4.9
		[0.14, 0.2, 0.14, 0.52]	22.1	19.3	24.0	28.7	38.4	0.2	1.4	1.5	2.2	4.7
		[0.14, 0.28, 0.14, 0.44]	25.6	22.1	27.4	34.4	45.7	0.2	1.4	1.6	2.3	5.2
	GA	[0.04, 0.12, 0.04, 0.8]	24.9	21.0	26.9	32.6	41.2	0.6	1.4	1.7	2.3	3.7
		[0.04, 0.22, 0.04, 0.7]	22.5	20.2	25.3	30.9	38.4	0.6	1.5	1.4	2.1	3.8
		[0.1, 0.2, 0.1, 0.6]	20.8	18.1	22.8	27.9	35.8	0.5	1.4	1.6	2.1	3.0
		[0.14, 0.2, 0.14, 0.52]	22.1	19.3	24.5	29.5	37.1	0.5	1.4	1.6	2.1	3.4
		[0.14, 0.28, 0.14, 0.44]	25.6	22.1	27.9	35.0	43.7	0.6	1.6	1.6	2.2	3.0
SAD	CIP	[0.04, 0.12, 0.04, 0.8]	27.8	24.8	26.4	–	–	0.2	17.2	110.7	>300	>300
		[0.04, 0.22, 0.04, 0.7]	25.3	22.4	25.0	–	–	0.2	17.5	108.5	>300	>300
		[0.1, 0.2, 0.1, 0.6]	23.2	20.6	22.5	–	–	0.2	18.0	105.2	>300	>300
		[0.14, 0.2, 0.14, 0.52]	26.1	23.5	25.4	–	–	0.2	17.9	105.8	>300	>300
		[0.14, 0.28, 0.14, 0.44]	29.1	26.0	27.5	–	–	0.2	18.4	107.4	>300	>300
	CCP	[0.04, 0.12, 0.04, 0.8]	27.7	23.8	28.5	36.5	49.6	0.2	1.5	2.4	2.3	4.8
		[0.04, 0.22, 0.04, 0.7]	25.6	22.2	26.9	34.1	46.0	0.2	1.6	2.2	2.1	5.1
		[0.1, 0.2, 0.1, 0.6]	23.2	20.6	24.6	31.1	42.2	0.2	1.5	2.0	2.1	4.5
		[0.14, 0.2, 0.14, 0.52]	26.6	23.9	27.8	35.3	47.6	0.2	1.5	2.0	2.2	4.8
		[0.14, 0.28, 0.14, 0.44]	28.4	25.5	30.4	38.2	51.8	0.2	1.6	2.2	2.2	4.5
	GA	[0.04, 0.12, 0.04, 0.8]	27.7	25.3	29.9	38.2	47.4	0.7	1.5	2.4	2.1	3.9
		[0.04, 0.22, 0.04, 0.7]	25.5	24.2	27.9	35.9	44.1	0.7	1.7	2.2	2.3	3.5
		[0.1, 0.2, 0.1, 0.6]	23.2	21.6	25.3	32.4	40.9	0.7	1.5	2.0	2.1	3.0
		[0.14, 0.2, 0.14, 0.52]	26.7	25.0	29.0	37.3	45.9	0.7	1.5	2.0	2.1	3.4
		[0.14, 0.28, 0.14, 0.44]	28.5	26.7	31.4	40.5	50.0	0.7	1.6	2.0	2.0	3.5
NSOB	CIP	[0.04, 0.12, 0.04, 0.8]	23.9	23.0	20.2	–	–	0.2	15.7	115.5	>300	>300
		[0.04, 0.22, 0.04, 0.7]	21.8	21.1	18.3	–	–	0.2	17.2	114.8	>300	>300
		[0.1, 0.2, 0.1, 0.6]	21.5	20.1	18.0	–	–	0.2	17.0	110.1	>300	>300
		[0.14, 0.2, 0.14, 0.52]	23.3	21.3	19.0	–	–	0.2	16.8	110.0	>300	>300
		[0.14, 0.28, 0.14, 0.44]	24.0	22.8	20.2	–	–	0.2	16.8	115.2	>300	>300
	CCP	[0.04, 0.12, 0.04, 0.8]	24.4	22.5	24.6	29.3	42.8	0.2	1.3	2.3	2.8	6.7
		[0.04, 0.22, 0.04, 0.7]	22.4	21.1	21.9	27.2	38.3	0.2	1.3	2.3	2.4	7.2
		[0.1, 0.2, 0.1, 0.6]	21.5	20.1	21.5	26.5	38.1	0.2	1.4	2.3	2.6	5.8
		[0.14, 0.2, 0.14, 0.52]	22.5	21.2	22.5	27.7	40.1	0.2	1.4	2.3	2.6	6.4
		[0.14, 0.28, 0.14, 0.44]	24.7	23.0	24.5	29.9	42.6	0.2	1.4	2.4	2.7	6.1
	GA	[0.04, 0.12, 0.04, 0.8]	24.5	23.5	25.7	30.1	43.1	0.6	1.5	2.1	2.7	4.1
		[0.04, 0.22, 0.04, 0.7]	22.1	22.0	23.0	27.3	40.6	0.6	1.4	2.2	2.2	3.9
		[0.1, 0.2, 0.1, 0.6]	21.5	21.0	22.5	26.7	38.9	0.6	1.5	2.1	2.5	3.2
		[0.14, 0.2, 0.14, 0.52]	23.2	22.7	23.4	28.4	40.5	0.6	1.4	2.1	2.5	3.8
		[0.14, 0.28, 0.14, 0.44]	24.2	24.4	25.8	29.7	43.2	0.6	1.4	2.1	2.5	4.1
SADNSOB	CIP	[0.04, 0.12, 0.04, 0.8]	32.7	28.6	30.4	–	–	0.2	22.5	110.2	>300	>300
		[0.04, 0.22, 0.04, 0.7]	30.0	27.1	27.8	–	–	0.2	19.7	112.0	>300	>300
		[0.1, 0.2, 0.1, 0.6]	26.5	23.7	24.9	–	–	0.2	19.5	108.5	>300	>300
		[0.14, 0.2, 0.14, 0.52]	28.9	25.9	26.5	–	–	0.2	19.8	109.5	>300	>300
		[0.14, 0.28, 0.14, 0.44]	31.4	27.8	29.5	–	–	0.2	20.4	112.5	>300	>300
	CCP	[0.04, 0.12, 0.04, 0.8]	32.5	29.1	32.3	41.8	54.7	0.2	1.8	2.7	2.8	5.9
		[0.04, 0.22, 0.04, 0.7]	29.9	27.2	29.6	39.6	50.7	0.2	1.7	2.4	2.7	5.8
		[0.1, 0.2, 0.1, 0.6]	26.5	23.7	26.5	34.8	44.8	0.2	1.7	2.5	2.8	6.0
		[0.14, 0.2, 0.14, 0.52]	28.9	25.5	28.5	37.3	48.2	0.2	1.7	2.4	2.8	6.1
		[0.14, 0.28, 0.14, 0.44]	31.5	28.1	31.2	40.5	52.5	0.2	1.7	2.5	2.7	6.0
	GA	[0.04, 0.12, 0.04, 0.8]	31.9	29.1	33.3	42.1	50.5	0.7	1.9	2.5	3.1	4.2
		[0.04, 0.22, 0.04, 0.7]	30.3	27.6	30.3	38.7	46.7	0.7	2.0	2.4	2.7	4.1
		[0.1, 0.2, 0.1, 0.6]	26.5	24.1	27.2	34.8	42.1	0.7	1.9	2.4	2.6	4.0
		[0.14, 0.2, 0.14, 0.52]	28.1	26.2	29.6	37.8	44.6	0.7	2.0	2.5	2.8	4.1
		[0.14, 0.28, 0.14, 0.44]	31.0	28.0	31.6	41.2	48.6	0.7	2.2	2.5	2.8	4.0

IP can solve the small size problem to optimality when $|I|$ is 6, 12, and 18. CPLEX CP is used as a heuristic to obtain a solution and can also solve the problem to optimality when I is 6 and 12. The modified GA has insignificant deviations from the optimal solutions and performs well.

The results show that the overall variation in each model's objective function when changing the weights is reasonable and remains within 20%. It is also observed that the model yields higher values when the weights for the number of unscheduled patients are kept high or low. For example, when the weights for the number of unscheduled patients are kept low, the model will not be forced to schedule more patients, this may lead to higher idle times, increasing the value of the objective function. When the weights for the number of unscheduled patients are kept high, the model will schedule more patients, increasing waiting time and resource overtime. Table 3 indicates that the following weights – 0.1 for overtime, 0.2 for waiting time, 0.1 for idle time, 0.6 for the number of unscheduled patients – provide better results than the other weights experimented in the computational analysis. When $|I|$ increases, the objective function values first go down and then go up because scheduling more patients decreases idle time without significantly impacting waiting time and overtime. However, waiting time, overtime, and the number of unscheduled patients start increasing when $|I|$ is greater than 12, thus causing the objective function values to decline.

Patient no-shows and overbooking increase the objective function values because (1) the patient waiting time and resource overtime in the NSOB model are higher than the DET model, and (2) the impact of unscheduled patients on the objective function is relatively small when $|I|$ is low. Individual stochastic appointment durations in SAD increase the objective function values, which may be attributed to predicted appointment durations being more than the deterministic ones due to rounding them to the nearest integer, thus decreasing the number of unscheduled patients. SADNSOB generates the highest objective function values because overbooking and individual stochastic appointment durations increase waiting time and overtime without yielding a substantial decline in the number of scheduled patients.

It is shown that CIP can solve small outpatient chemotherapy scheduling problems but cannot be utilized to schedule more than 18 patients due to its computational complexity and long run time. The proposed GA generates similar results to CCP and can run reasonably faster. The computation time difference between the CCP and GA becomes more significant when the patient size $|I|$ increases. For example, when $|I| = 30$, we observe that GA performs as well as CCP and runs much faster than CCP across all models. Thus, we recommend that the proposed GA should be selected to create daily patient schedules for large problems.

After validating the optimization models, we use them to formulate a real appointment scheduling problem in which 240 patients need to be scheduled for a given day. The clinical pathway distribution for these 240 patients reflects the clinical pathway distribution provided in Fig. 7. The weights of the objective function are selected as 0.10 for overtime, 0.20 for waiting time, 0.10 for idle time, and 0.60 for the number of unscheduled patients based on the results of the small problem. Clinical pathways, appointments, resources, and capacities used in the big problem are given in Table 4.

The large scheduling problem above is formulated using the four optimization models and repeatedly solved 50 times using the modified GA approach with an average computation time of 206 min per model. The four objective functions (Z_1, Z_2, Z_3, and Z_4) obtained from repeating the modified GA 50 times for *each model are* plotted using a box plot, as shown in Fig. 10. The crossover and mutation rates in the GA are key elements to success to find the optimal or near optimal solutions. Hence, the experiment uses different sets of crossovers (.7, .8, .9) and mutation (.001, 0.05, 0.01) rates to ensure the results obtained from the GA are accurate and reliable. The results indicate that the crossover rate of 0.9 and mutation rate if .001 generate the best outcomes.

The boxplots indicate that DET and SAD models schedule fewer patients than NSOB and SADNSOB, which is expected as overbooking is not allowed in the DET and SAD models. This is a significant improvement over DET and SAD because timely access to care is critical for cancer patients. The patients scheduled using the DET and NSOB models have more waiting time than the SAD and SADNSOB models because the DET and NSOB models use fixed timeslots for MDCAs, MDFAs, and LTAs and distribute the ITA durations among patients discretely while SAD and SADNSOB utilizes individualized appointment durations obtained from the ANN_α models. It is also observed that there are less idle time and more overtime in the optimization models that use overbooking (i.e., NSOB and SADNSOB), which is probably due to scheduling more patients for a given day.

It is critical to note that these results may not reflect what happens in a real setting. For example, if the clinic uses the DET or SAD model to create daily schedules, the idle time could be much higher as there may be no-show patients. Schedules created using SAD and NSOB models may not work as expected in terms of waiting time and overtime in a real setting owing to actual appointment durations being drastically different from the deterministic appointment durations used in DET and NSOB models. Thus, there is a need to conduct an experimental analysis through simulation to report how these schedules will perform in a real-life scenario.

Table 4
Clinical pathways, appointments, resources, and capacities.

Appointment type	Resource type	Capacity	Deterministic duration $T_{i\alpha}$ in timeslots & number of patients that uses deterministic duration $T_{i\alpha}$
MDCA MDFA	MD	8	3 (240) 2 (240)
LTA	LAB	5	3 (240)
INT	RN	5	3 (12), 6 (48) 12 (60), 18 (52), 24 (28), 30 (24), 36 (10), 42 (3), 48 (3)

5.3. Experimental analysis

A simulation analysis is conducted to identify the impact of patient no-shows, overbooking, and individual stochastic appointment durations on KPIs. Four simulation models are built in Simio® using the dataset described previously to represent the four optimization models (i.e., DET, NSOB, SAD, SADNSOB). Each simulation model uses the patient schedule generated by the optimization model that it represents. The simulation results acquired from DET are analyzed to identify the impact of patient no-shows without the overbooking strategy. Then, the simulation results of the DET and NSOB are compared to assess if overbooking is a viable strategy to reduce the adverse effects of patient-no shows. The results of DET and SAD are compared to observe if incorporating individual stochastic appointment durations enhances the KPIs. Finally, SADNSOB is used to determine if concurrently accounting for patient no-shows, overbooking, and individual stochastic appointment durations is worth the effort.

The large optimization problems with 240 patients are solved, and patient schedules are obtained. The scheduled patients go through their sequence of appointments based on their pathway, starting from their first appointment in the simulation models, as given in Table 1. The patients are assumed to be on time for their first appointment. There are four processes in the simulation model, each of which represents an appointment type, such as MDCA, MDFA, LTA, and ITA. The resource capacities of the processes are set to be the same as the large optimization problem, as provided in Table 4. The appointment durations in all the simulation models are computed via the ANN models. To account for stochasticity in the simulation model and represent the operations and workflow more accurately, the appointment durations are set to vary uniformly between 80% to 120% of the appointment durations calculated using the ANN_α models. We vary the appointment durations by 20% because the errors obtained from the ANN_α models are within the range of 20% of the actual appointment durations. For example, if ANN_{ITA} computes Patient 1's infusion appointment duration T_{1ITA} as 18 timeslots, the simulation model will uniformly generate a random number between (18).(0.8) = 14.4 and (18).(1.2) = 21.6 timeslots and convert it to minutes. Then, Patient 1 and the RN assigned to the ITA of Patient 1 will be kept busy for this generated time.

Since patient no-shows happen in real life, the simulation models incorporate the no-show probabilities for the scheduled patients. The no-show probabilities are computed using the ANN_{PNS} model and then compared to a number generated randomly between 0 and 1. If

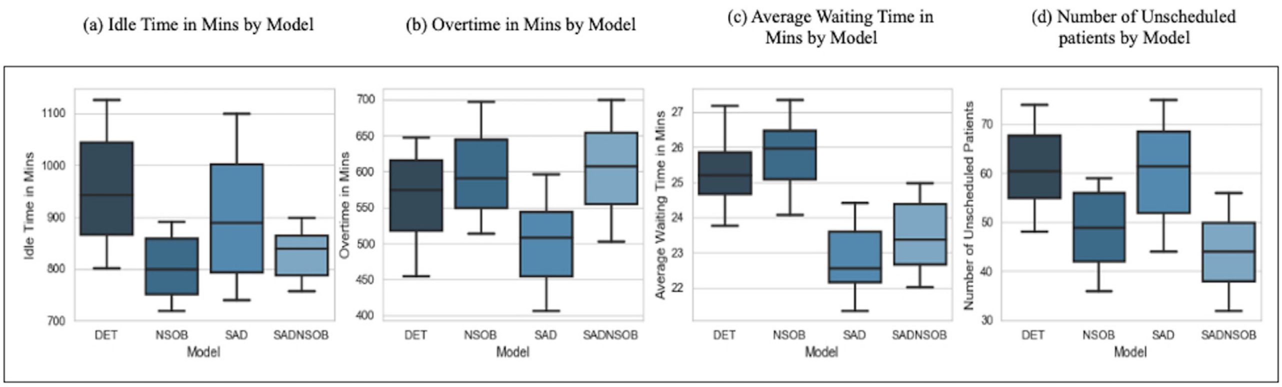

Fig. 10. Results of modified GA.

Table 5
Simulation model validation.

Metric	Simulated		Actual	
	Mean	95% Confidence interval (CI)	Mean	95% Confidence interval (CI)
Average waiting time	29.23	(28.88–29.58)	30.54	(25.37–35.71)
Average completion time	129.61	(122.52–136.70)	135.17	(121.93–144.41)
Average overtime	61.21	(57.32–65.10)	64.87	(59.13–70.61)

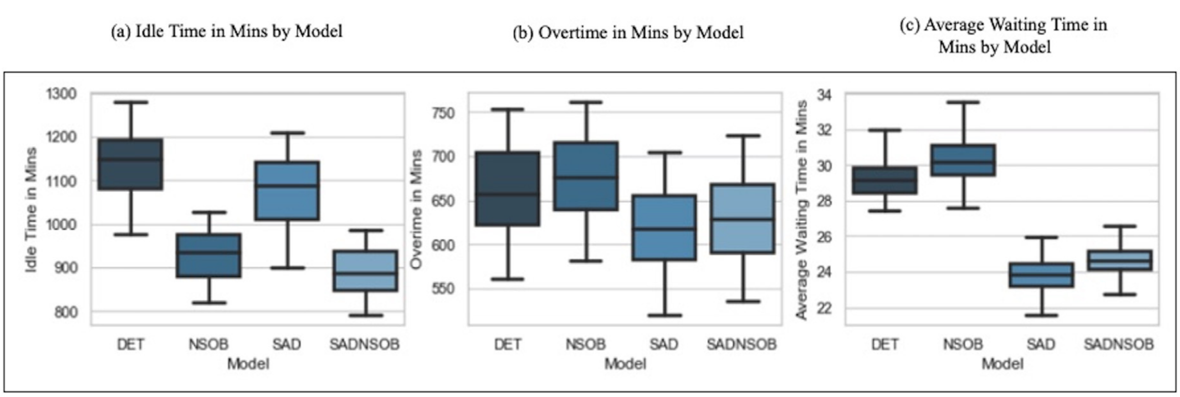

Fig. 11. Simulation results — KPIs by model.

the patient's no-show probability is higher than the randomly generated number, he/she is assumed to be a no-show in the simulation models.

We follow the patients scheduled using the DET model in the clinic and record several variables, such as their arrival times, start and end times of their appointments, and the resources they use. Using these variables, several metrics, including total patient waiting time, resource overtime, average completion time, representing the time between patient arrival and departure from the clinic, are computed. Then, these actual metrics are compared with the simulated metrics. Table 5 summarizes these three metrics obtained by simulating the patient schedules of the DET model. The overlapping confidence intervals for these metrics indicate that the simulation model accurately represents the clinic. Resource idle time is not captured during the data collection process due to not being able to reliably observe the resources throughout the day.

The simulation models are replicated 50 times to conduct statistical analyses. The results of KPIs obtained from the simulation models are summarized in Fig. 11 using boxplots for easy comparison. Instead of total waiting time, the average waiting time per patient is reported because it provides an objective comparison among the models.

Fig. 11 and Table 6 show that the resources have significantly more idle time when the patient schedules obtained from the DET and SAD models are used as compared to the NSOB and SADNSOB because the former models do not preemptively account for patient no-shows and do not consider the overbooking strategy. It is also observed from the simulation results that the resources in the DET and SAD models do not have significantly less overtime than the NSOB and SADNSOB models despite the latter scheduling more patients because of overbooking. The differences in average patient waiting time among these models are minimal, despite being statistically significant. These findings indicate that incorporating overbooking while creating patient schedules is a viable strategy to avoid the adverse effects of patient no-shows.

The impact of using individual stochastic appointment durations can also be obtained from the simulation results, as given in Fig. 12 and Table 6. The SAD model yields better idle time, overtime, and average waiting time as compared to DET. Similarly, SADNSOB gives better performance than NSOB in terms of idle time, overtime, and average waiting time. These results strongly suggest that accounting for variations in appointment durations preemptively and creating patient schedules accordingly result in better KPIs, highlighting the effectiveness of using individual stochastic appointment durations obtained from the ANN_α models.

Fig. 12 breaks down the results to the resource level. The results illustrate that the resources in downstream operations, such as MD and LAB, have consistently more idle time in the DET and SAD models. However, their overtime is not significantly less than the NSOB and

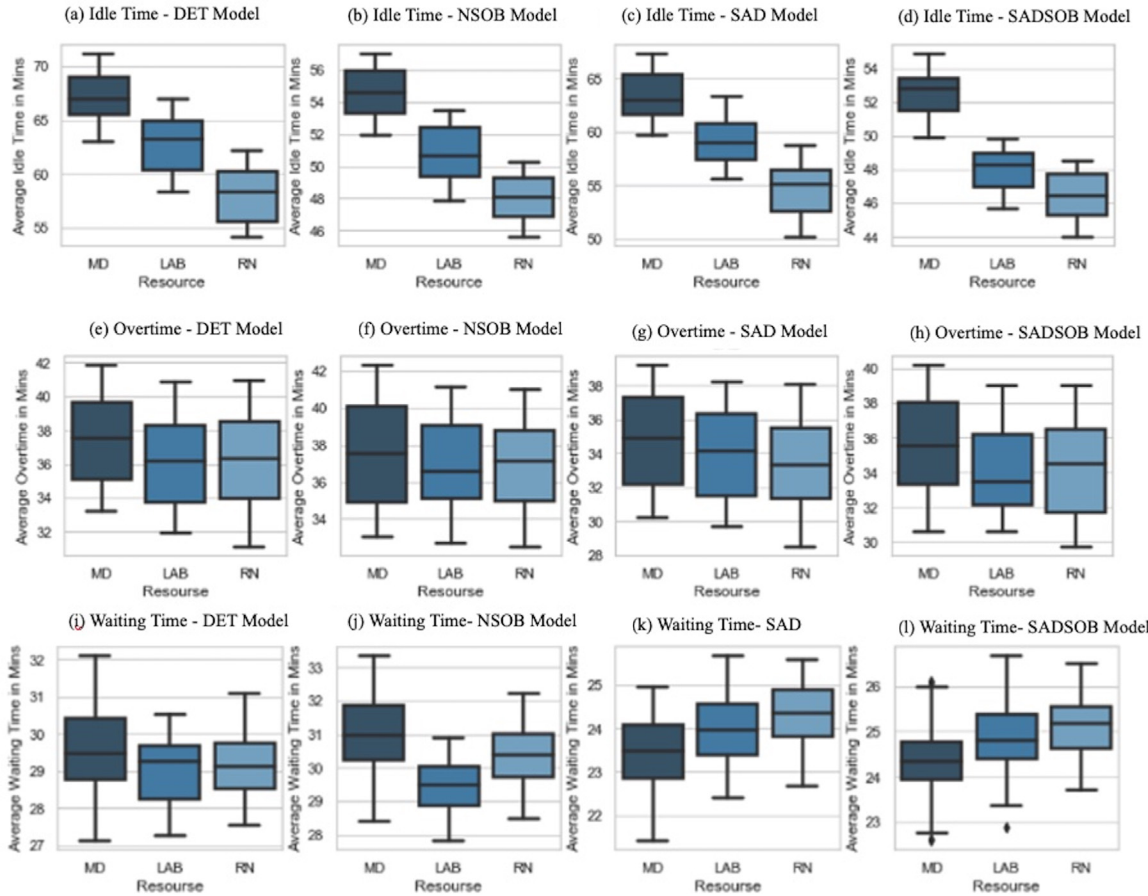

Fig. 12. Simulation Results KPIs by resource and model.

SADNSOB models, respectively. These observations are aligned with an earlier finding from the ANN_{PNS} model, stating that patients with only an MDCA or LTA are more likely to no-show. Therefore, clinics that do not use the overbooking strategy to address patient no-shows can schedule patients with ITA appointments early in the day. Then, the clinic can assign patients only with an MDCA or LTA later in the day, allowing idle time to occur late in the working hours without significantly increasing the resource overtime. Another interesting observation is that using individual stochastic appointment durations improves waiting time for each resource type, even when overbooking is utilized.

Table 6 statistically compares the results obtained from the simulation models. The baseline model DET poorly performs as compared to other models. For example, NSOB statistically gives better idle time than the DET, and overtime of NSOB is not statistically different than of DET. This result suggests that there is a need to consider patient no-shows when creating patient schedules. Additionally, overbooking does not cause further congestion and is not destructive to quality of care if implemented using historical data and patient no-show probabilities. Using individual stochastic appointment durations provides statistically significant improvements across all KPIs. SADNSOB outperforms the other models, thus demonstrating that consideration of patient no-shows, overbooking, individual stochastic appointment durations enhance the KPIs and helps schedule more patients, providing improved access to care.

Table 6
T-test to compare the models (sample size: 50 & significance level: 0.05).

Student t-test steps	Models	Idle time	Overtime	Average waiting time
MEAN of KPIs by model	DET	1138.60	660.81	29.23
	NSOB	927.00	675.60	30.29
	SAD	1076.90	617.52	23.84
	SADNSOB	890.72	629.07	24.65
Standard deviation of KPIs by model	DET	79.13	49.68	1.26
	NSOB	56.66	47.89	1.41
	SAD	84.23	45.39	1.37
	SADNSOB	53.09	48.58	1.21
P values for mean differences $\neq 0$	DET-NSOB	0.00	0.13	<0.01
	DET-SAD	<0.01	<0.01	0.00
	NSOB-SADNSOB	<0.01	<0.01	0.00
	SAD-SADNSOB	0.00	0.22	<0.01

6. Conclusions & discussions

This research utilizes machine learning and optimization models and considers patient no-shows, overbooking, and individual stochastic appointment durations to schedule outpatient chemotherapy visits with multiple appointments. The study makes four significant contributions to the existing body of literature: (1) It tackles the appointment outpatient chemotherapy scheduling as a problem of coordinating multiple resources across various clinical pathways with multi-appointments, (2) it considered patient no-shows and overbooking, (3) it incorporates individual stochastic appointment durations, (4) it showcases how the use of machine learning (i.e., ANN) can enhance prescriptive modeling (i.e., optimization).

The study builds five ANN models. The ANN_{PNS} model is used to predict patient no-show probabilities, while the ANN_{MDCA}, ANN_{MDFA}, ANN_{LTA}, ANN_{ITA} models are applied to predict individual appointment durations. This research develops four optimization models – DET, NSOB, SAD, and SADNSOB – to schedule outpatient chemotherapy patients with multiple appointments. The results obtained from these models are compared to extract the impact of overbooking and individual stochastic appointment durations on KPIs.

The results of the ANN_{PNS} model indicate that patients who book their appointments well in-advance have higher no-show probabilities. The ANN_{PNS} model finds out that *"Adult Household"* and *"Age"* may define patients' mobility and be used to identify patients with higher no-show probabilities. The ANN_{PNS} model illustrates that *"Appointment Type"* affect patient no-shows. Patients who visit the clinic for MDCA, MDFA, or LTA are more likely to no-show as compared to patients who visit the clinic for ITA.

Several managerial implications can be deduced from the ANN_{PNS} model. (1) Additional reminders must be sent to patients. Specifically, patients who book their appointments in advance and do not confirm their appointments should be given a phone call. (2) Transportation services should be offered by clinics so that patients who have difficulty traveling to or from the clinic can make it to their appointments. (3) An intervention program that helps educate the patients about the importance of receiving chemotherapy treatments on time should be provided. During this program, patients should be introduced to techniques that will help them cope with distress that may lead them to miss their appointments.

A large appointment scheduling problem with 240 patients is formulated using the four optimization models and solved with the modified GA approach. Then, the patient schedules obtained from these optimization models are assessed through simulation analysis. The simulation results indicate that considering patient no-shows and overbooking reduces the number of unscheduled patients without significantly increasing patient waiting time and resource overtime. The simulation analysis shows that the models without overbooking – DET and SAD – yield more idle time in the downstream resources (i.e., MD and LAB) because patients without ITA are more likely to no-show than the patients with ITA. Thus, if clinics do not want to employ an overbooking strategy to combat patient no-shows, patients without ITA should be scheduled later in the day, allowing idle time to occur late in the working hours without significantly increasing the resource overtime. Employing individual stochastic appointment durations computed from the ANN_{α} models give a more realistic patient schedule and yields better KPIs. Particularly, using individual stochastic appointment durations decreases resource overtime and patient waiting time, which may, in return, improve employees' morale and patient satisfaction.

To sum up, overbooking patients based on ANN_{PNS} reduces the adverse effects of patient no-shows. Additionally, overbooking provides cancer patients with timely access to chemotherapy, which is critical for treatment. Using individual stochastic appointment durations when scheduling patients is an effective strategy to improve KPIs due to generating more realistic patient schedules and allowing better resource utilization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data that has been used is confidential.

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