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Home-based care and center-based care: From being alternatives to being synergistic. Optimization models to support flexible care delivery☆

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ABSTRACT

The delivery of health care services, especially for patients with chronic conditions and/or requiring cyclical treatment, can be accomplished by resorting to two organizational models: center-based care and home-based care. In developed countries, government pressure to reduce healthcare spending and the COVID-19 pandemic have led to the spread of home-based care. This type of care is proven to outperform the center-based one in terms of cost-effectiveness, patient satisfaction, and adherence to treatment guidelines. However, even for treatments usually suitable to be delivered at home, the patient's health status or other constraints may make it inappropriate to deliver service at the patient's home. This calls for a new organizational model, referred to as flexible care, where home-based and center-based care are not seen as mutually exclusive models but as options that can be activated according to the patient's and provider's needs. This paper presents a novel network-based deterministic optimization model and two matheuristics to address a scheduling problem typically faced by providers adopting a flexible care model. The model considers a provider relying on a treatment room with a fixed number of medical chairs, a fleet of vehicles, and a team of operators. It allows for determining on which days of the planning horizon, in which setting (home or center), and by which operator each patient will be treated. The model takes into account patients' preferences and considers two objective functions: minimizing provider costs and patients' travel time. In addition, we propose a two-stage mixed-integer stochastic programming model with recourse actions. This model allows incorporating the uncertainty due to the occurrence of adverse events. Adverse events are sudden changes in the patient's condition randomly happening at a specific point in the planning horizon. These events render the patient unsuitable for home care and require them to be visited at the center from that moment onward. The models have been inspired by a real case and tested on multiple random instances.

1. Introduction

The delivery of health care services, especially in the case of patients with chronic conditions and/or requiring cyclical treatment, can be accomplished by resorting to two ideal-typical organizational models once seen as alternatives: the center-based care (CBC) one, consisting of patients receiving services at the server facility, and the home-based care (HBC) one, involving health workers providing services at patients' home. In developed countries, pressure from governments to reduce healthcare spending in the face of an ever-increasing aging population and social changes has increasingly driven the use of the HBC model [1–4]. Furthermore, the COVID-19 pandemic and the associated need to control hospitals' capacity [5] and clinical risk further contributed to this trend. Especially in the case of long-term care, HBC is proven to outperform the CBC in terms of cost-effectiveness [6,7], patient satisfaction [8], and adherence to treatment guidelines [9]. In addition, it allows for saving hospitals' capacity for acute care treatment.

Programs that reduce the burden of travel by bringing care to the patient's home or workplace, or satellite/mobile clinics closer to home, are spreading rapidly around the world as they have been shown to increase treatment capacity and improve patient satisfaction [10,11].

However, even for treatments usually suitable to be delivered at home, the patient's health status (e.g., comorbidities, allergies, possible

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adverse reactions to certain drugs) or other constraints (e.g., a lack of proper housing, absence of informal caregivers) sometimes makes it impossible or impractical to deliver service at the patient's home. In such an increasingly complex landscape, healthcare providers must decide not only the type of care plan each patient should follow but also the setting (HBC or CBC) in which it should be delivered, even for patients with the same disease. This complexity calls for a new organizational model, hereafter referred to as Flexible Care (FC), where HBC and CBC are seen as options that can be activated depending on the patient's and provider's needs [10].

This paper presents a (deterministic) novel network-based optimization model to address a scheduling problem typically faced by providers adopting an FC model and a two-stage mixed-integer stochastic programming model with recourse actions, stemming from the deterministic one, which allows for the incorporation of uncertainty due to the occurrence of *adverse events*. An adverse event is an unexpected event (like falls, injuries, infections, adverse drug reactions, as well as psychological harms) causing a sudden deterioration in the patient's condition at a certain point of the time horizon, that renders them unsuitable for home care and requires them to be serviced at the center from that moment onward [12,13]. These types of events may require the provider to reallocate and/or commit new resources to accommodate changing patient needs. This can severely harm the provider's performance. The stochastic model was created to strengthen the robustness of schedules when dealing with adverse events.

The deterministic model considers a provider that can rely on an equipped treating room (hereafter referred to as the *center*) with a fixed number of medical chairs (e.g., clinical, infusion, chemotherapy chairs) located in a hospital or outpatient clinic, a fleet of vehicles, and a team of operators who can be deployed either at the center or on-field. Such a provider needs to assist a set of patients requiring the *same type of cyclical treatment* (i.e., a treatment dispensed with a given periodicity such as infusions) and may or may not be eligible for home care over a medium to a long period. The model allows for determining on which days of the planning horizon the center will be reserved for the administration of a given type of treatment, in which setting (home or center), and which operator will serve each patient. The model considers patients' preferences as well. We consider two objective functions (OFs). The first one (OF_1) minimizes the provider costs, which include center costs, operator costs, and travel costs (provider-centered approach). The second one (OF_2) minimizes the patients' travel time (patient-centered approach) under the condition that the overall cost of the solution does not increase from the optimal value of OF_1 beyond a threshold deemed acceptable.

The stochastic model, in the first stage, mirrors the deterministic one. In the second stage, i.e., after adverse events become known, cost minimization is achieved through two recourse actions: *resource overloading* and *resource activation*. Resource overloading implies using operators already scheduled to work at the center on certain days to visit patients who are reassigned from home care to the center on those same days due to an adverse event. Overloading can result in overtime when operators are required to work beyond the end of their scheduled shift to attend to patients reassigned to them. Resource activation, instead, entails activating additional resources, including operators and the center, to attend to patients at the center when it wasn't initially booked for the same service. The stochastic model's objective function accounts for the total expected cost for the providers and includes center cost, operators' costs, and travel costs as well as the overtime and resource activation costs.

The models have been inspired by a real case and tested on multiple random instances.

This study contributes to both theory and practice. Indeed, while the healthcare literature abounds with models supporting decisions in the CBC and HCB settings, to the best of our knowledge, there are neither models explicitly dealing with the FC setting, nor models addressing the uncertainty arising from adverse events in home care.

Nonetheless, determining which patients to serve at home or at the center and coordinating field activities with those at the center are both topical and relevant problems. Community-based centers providing both center-based and home care services to a local population are spreading, at least in the EU, partly as a result of the National Health System reforms promoted in many countries after the COVID pandemic [14]. Optimizing the operation of these structures will, therefore, be essential to ensure health systems' sustainability and efficiency. In this regard, it is worth noting that adverse events can cause significant disruption, hence, taking into account their possible occurrence can considerably facilitate the implementation of the optimization model solution in real-world contexts. This paper is organized as follows. Section 2 reviews the literature. Section 3 describes the problem addressed and the notation adopted. Section 4 presents the deterministic models developed, while Section 5 describes the stochastic model. Section 6 introduces the experimental campaign conducted, Section 7 shows and discusses the results achieved, and Section 8 summarizes the main findings from a managerial perspective. Finally, Section 9 reports the study's conclusions and limitations and proposes avenues for future research.

2. Literature review

Literature dealing with health service planning typically supports decisions such as (i) resources allocation (chairs, beds, devices, rooms, etc.), (ii) assignment of operators to patients, (iii) appointment scheduling (i.e., determining day and time when a service is provided), (iv) staff rostering, and (v) routing of operators or transportation of patients. The first four types of decisions concern both CBC and HBC settings, while routing decisions are more common in HBC, even if they have recently been studied in CBC settings as well [10]. These decisions are strongly intertwined and give rise to complex optimization problems that are often difficult to solve, even for medium-scale instances. For this reason, the literature abounds of works that consider only some of the above decisions [15–17] or that propose multi-stage methods in which decisions are made in a cascade [18,1,19–21]. However, recently, thanks to the pattern-based methodology first introduced by Cappanera and Scutellà [22], there has been an increase in works dealing with an ever-increasing number of decisions simultaneously [23] up to Naderi et al. [24] who deal with all the five above-mentioned decisions, while also addressing the uncertainty of travel and service times. Reviewing the massive amount of literature supporting decision-making in either CBC or HBC settings is out of the scope of this paper. Instead, we refer the reader to [25] for more details about the HBC setting and to [26] for the CBC one (here, the most frequently addressed problem is appointment scheduling). It is worth pointing out, however, that the rapid spread of home care services over the past decade has prompted the production of a significant number of studies considering an increasing number of features, e.g. multimodal transportation [27], complex timing and synchronization constraints of operators [28], shared management of equipment by operators [29], continuity of care or loyalty [30,31] and regularity of service [32] as well as various sources of uncertainty. These include: uncertainty concerning service demand [33,34,23,35], service time [36,37,20,38], both service and travel times [39,40,37], caregiver availability [41], and corporate social responsibility issues including employment opportunities and regional economic development [42].

As for the OFs employed, most of them are provider-oriented and concern, for example, the minimization of travel time/cost/distance [43,44], overtime costs [43,45], or treatment duration/working time [46,31]. Others are more patient-oriented [47,25] and concern, for example, the maximization of the total priority of the treated patients [48], the fulfillment of patient preferences [31,49], and the achievement of continuity of care [30,31]. Finally, staff-oriented OFs exist, too, and typically aim to achieve workload balancing across operators [33,30].

Despite the relevant number of features that the models currently available in the CBC and HBC literature allow for consideration, scheduling problems in the FC setting have not been investigated yet. In addition, no study other than [50] has considered the uncertainty related to the potential onset of adverse events to date. Such a study, however, deals with real-time scheduling problems and not, like ours, with a medium-term planning problem.

This paper aims to address these gaps by focusing on a medium-term planning problem comprising aspects of resource allocation, assignment, appointment scheduling, and routing and by dealing with the uncertainty caused by adverse events. The next section describes the problem in detail.

3. Problems description and notation

3.1. Problem description

We consider a provider who, over a medium to long planning horizon (e.g., three months), has to cyclically administer the same type of treatment to a set of patients. The standard duration of the treatment session and the standard time between two consecutive treatment sessions can vary across patients, but it is fixed, for each patient, in the planning horizon. Treatment times are not subject to a significant variation (as is typically the case of infusion therapies or physiotherapy sessions).

Depending on the treatment and the patient's status, a deviation from the standard time between two sessions may or may not be accepted within a certain tolerance (e.g., ± 1 day). The treatment can be administered at the center or the patient's home, and its duration depends on the patient's treatment plan, not on the setting.

On a given day, to *treat patients at the center*, the provider must book the center for the whole day. This choice aims to avoid setting up the center more than once a day for different treatment types and simplify the scheduling of center activities. Moreover, it allows patients with the same condition to interact, share the problems related to their condition, and socialize. Patients treated at the center go to the center autonomously and occupy a medical chair and an operator for the duration of the treatment session.

To treat patients at home, instead, the operators need to pick up one of the provider's vehicles at the center, gather the material required to administer the treatment, treat all patients daily assigned to them, and return the vehicle to the center at the end of their tour. Homecare service is assumed to be delivered in a setting where travel times are relatively short, affected by modest variability, and known a priori.

The number of available operators, medical chairs, and vehicles is fixed in the planning horizon.

The duration of each treatment session does not depend on the setting where the treatment is administered. The distances and travel times between each pair of patients and between the patients and the center are known a priori.

All patients can be served at the center, but not all of them are also eligible for home care. If a patient is assigned to home care (center care), they will be seen at home (at the center) for all the planning horizon, unless they will be affected by an adverse event, in which case they need to be rescheduled at the center, for the rest of planning horizon.

Each operator can treat patients at both the center and home, but each day an operator is assigned either to home or center care. Each patient expresses a preference regarding the day on which to be seen (e.g., odd or even days). The provider commits to continuity of care and, therefore, ensures that the patient is always treated by the same or a limited number of operators. In fact, being treated by many different front-line operators has been proven to reduce trust in the provider and undermine patient satisfaction [51]. When the center is not reserved for the treatment under consideration and the operators are not scheduled at home, they can be engaged in the administration of other treatments either at the center or at home. Starting from this general problem, we studied two distinct though related problems, one *deterministic* and one *stochastic*.

The ***deterministic problem*** neglects the potential occurrence of adverse events (as well as any other form of uncertainty) and consists of determining (i) on which days of the planning horizon the center should be booked, (ii) on which day, (iii) in which setting (home or center), and (iv) by which operator, each patient should be served, and (v) for each day that operators are assigned to home care, the order in which they should treat patients assigned to them. The objective is to minimize the provider costs (OF_1, provider-oriented) or the patients' travel distance (OF_2, patient-oriented).

The ***stochastic problem,*** instead, considers that certain flexible patients (hereafter referred to as "affected patients") might undergo an unforeseen adverse event, necessitating their rescheduling at the center from the day of the event onwards. Both the patients experiencing the adverse event and the day when the event will occur are unknown. We hypothesize that to treat a patient at the center following an adverse event, the provider can either use operators who were already scheduled to work at the center on the days the patient is rescheduled or, if there are no scheduled visits for those days, activate new resources, such as operators and the center itself. In the first case, the provider could incur overtime costs as operators may need to extend their working hours beyond the originally scheduled shift. In the second case, the provider incurs the cost of activating extra operator and center capacity. The objective of the stochastic problem is to minimize the overall expected cost for the provider, encompassing center costs, operator costs, travel costs, and additional expenses related to overtime and resource activation.

3.2. Notation

This section introduces the notations we use in all models presented in the remainder of this paper. We adopt a network representation to model the sequencing of each patient's treatment sessions over the planning horizon. Thus, we have a graph $G^p = (N^p, A^p)$ associated with patient p, with N^p defining the set of nodes and A^p the set of arcs. Specifically, the set of nodes contains a node for each day in the planning horizon D in which patient p can receive the service (D^p). This set is built by filtering from D the days that are suitable for the patient considering the day (l_p) on which the patient received the last service in the past, the standard time between two consecutive treatment sessions (μ_p) and the tolerance (ε_p). Thus, the resulting set D^p depends on the specific patient. Additionally, the node set includes the root node (r) and the terminal node (t), i.e., $N^p = D^p \cup \{r, t\}$. The arc set A^p is made of three groups of arcs: (i) the arcs linking the root node with nodes corresponding to days on which the first treatment of the patient can occur, (ii) the arcs linking nodes corresponding to days on which the last treatment of the patient can occur with the terminal node, and (iii) arcs linking two nodes corresponding to days in which consecutive treatments can be provided to that patient. The scheduling of the treatments of patient p in D is thus described by a path leaving the root node, entering the terminal node, and touching, exactly once, the nodes corresponding to the days on which the treatments are provided.

To embed routing decisions in our model (see Section 4.4), we use dummy node r to denote the node where the tours of operators working in the home care setting start and end. The dummy node r is assumed to be the same for all the operators $o \in O$ and all the days $d \in D$. Tables 1 and 2, respectively, describe the notation used to identify the sets and the parameters, while Table 3 reports the decision variables. In the following, we use capital letters for sets, Greek letters for parameters, and Latin letters for variables. Fig. 1 provides a pictorial representation of the graph built for a hypothetical patient and gives examples of the notation used. The graph refers to a planning horizon of 6 weeks – 42 days corresponding to nodes numbered from 1 to 42. Sundays correspond to nodes labeled with multiples of 7. Nodes numbered with non-positive labels correspond to days in the previous programming period. Consider a patient p who had the last treatment on day $l_p = -8$. Then, with $\mu_p = 14$, and $\varepsilon_p = 0$, the first treatment must occur on day $d = 6$ $(-8 + 14)$, the second one on day 20, and so on. When $\varepsilon_p = 1$, a

Table 1
Sets.

Symbol	Set description	Value
D	Days in which service can be provided (working days)	{1, 2, …, d, …, |D|}
W	Weeks in D	{1, 2, …, w, …, |W|}, each week $w \in W$ is a set of days
S	Settings	{c=center; h=home}
P	Patients	{1, 2, …, p, …, |P |}
P^c	Patients who can receive the treatment only at the center	$P^c \subseteq P$
P^d	Patients $p \in P \backslash P^c$ who can receive the treatment on day d	$P^d \subseteq P \backslash P^c$
O	Operators	{1, 2, …, o, …, |O|}
S^p	Settings that are eligible for $p \in P$	$S^p \subseteq S$
D^p	Days in which $p \in P$ can receive treatment	$D^p \subseteq D$
U^p	Undesirable days for $p \in P$	$U^p \subseteq D^p$
A^p	Arcs in the graph of $p \in P$	(r, d) ∪ (d, d') ∪ (d', t)
K^p	Intervals in which patient p can receive treatment	{1, 2, …, k, …, $\|K^p\|$}, each interval k is a set of days
I_{pk}	Days in interval k in which patient p can receive a treatment	
E	Adverse event scenarios	{1, 2, …, e, …, |E|}
$\overline{O}$	Operators in O and an extra-resource $\overline{o}$ that could be activated to manage adverse events	O ∪ {$\overline{o}$}

Table 2
Parameters.

Symbol	Description	Scope
λ	Center daily cost	
η	Operator daily cost	
π	Travel cost per km	
θ	Maximum number of operators that can work at the center per day	
ρ	Maximum number of operators that can work in home care per day	
χ	Daily activation cost of the operator $\overline{o}$ (in the stochastic model)	
ζ	Hourly cost of overtime (in the stochastic model)	
ν	Percentage of patients experiencing an adverse event	
ε_p	Tolerance	$\forall p \in P$
μ_p	Standard time between two consecutive treatment sessions	$\forall p \in P$
ω_p	Maximum number of operators assigned to a patient in the planning horizon	$\forall p \in P$
σ_p	Maximum number of times a patient can be treated at home on an undesirable day	$\forall p \in P$
l_p	Day of the last treatment session	$\forall p \in P$
δ_p	Treatment time	$\forall p \in P$
ψ_p	Minimum number of treatments patient p must receive in D $\psi_p = \left\lfloor \frac{-l_p + \|D\|}{\mu_p} \right\rfloor$	$\forall p \in P$
Γ	Travel distance matrix with γ_{ij} distance from i to j (c=center)	$i,j \in P \cup \{c\}$
$\overline{\gamma_j}$	Mean travel distance to $j = \frac{\sum_{i \in P \cup \{c\}} \gamma_{ij}}{\|P\|}$	$\forall j \in P \cup \{c\}$
Φ	Travel time matrix with φ_{ij} travel time from i to j (c=center)	$i,j \in P \cup \{c\}$
$\overline{\varphi_j}$	Mean travel time to go to $j = \frac{\sum_{i \in P \cup \{c\}} \varphi_{ij}}{\|P\|}$	$\forall j \in P \cup \{c\}$
$\overline{\overline{\varphi}}$	Grand mean travel time $= \frac{\sum_{j \in P \cup \{c\}} \overline{\varphi_j}}{\|P\|}$	
α_o	Duration of operator shift	$\forall o \in O$
β_o	Maximum number of days each operator can work in a week	$\forall o \in O$
Δ	Maximum allowable cost increase when using OF_2	
u^e_{pd}	1 if in scenario e patient p on a day before d had an adverse event, 0 otherwise. (in the stochastic model)	$\forall e \in E, \forall p \in P \backslash P^c, \forall d \in D$
ξ_e	Probability of having the set of adverse events characterizing scenario e (in the stochastic model)	$\forall e \in E$

deviation of ± 1 day from the standard time between two treatments is acceptable as long as the resulting day belongs to the set of days D^p on which p can receive service. Thus, for example, the first treatment could occur on day 5, 6, or 7, but on day 7 (Sunday) the center is closed, thus resulting in $I_{p1} = \{5, 6\}$. A path starting from node r, entering node t, and touching exactly one node in each set I_{pk} defines the treatment schedule for p. As an example, according to path r-6–19–33-t, the three treatments required by p are scheduled on days 6, 19, and 33.

4. Deterministic models and solution approaches

To solve the deterministic problem described in the previous section, we propose and compare two alternative approaches, *two-phase* and *one-phase,* that differ in how they handle operator routing decisions.

With the two-phase approach, routing decisions are addressed in the second phase after the scheduling and allocation ones are made in the first phase. This reduces the computational complexity of the model and allows taking into account that in real-world settings, these decisions are often decoupled. While this decoupling may lead to suboptimal solutions on the theoretical level, it allows two problems of a different nature to be handled separately. Scheduling and assignment decisions must be made well in advance to allow patients and operators to organize their activities. The routing ones, instead, can be postponed so as to accommodate last-minute patients' or operators' needs. The two-phase approach, thus, in the first phase involves using an optimization model to determine on which days of the planning horizon the center should be booked and on which days, in which setting (home or center), and by which operator each patient should be served (*scheduling* and *assignment* decisions). Such a model uses approximated travel times and distances (more on this in Section 4.1). Then, the second phase involves determining the order in which the operators should visit their assigned patients (*routing* decisions) by solving a classic Travelling Salesperson Problem (TSP) [52,53]. The two-phase approach is implemented using, in the first phase, five different optimization model variants (see Section 6.2) sharing a common set of constraints (see Section 4.1). Specifically, starting from a baseline model (M_0), we create four variants (M_1, M_2, M_3, M_4) by adding some constraints or by changing the objective function (see Table 5). Two of these four variants (M_1, M_2) are matheuristics defined starting from the solution of a purposely defined set covering-like auxiliary model (AUX). Using AUX's solution to fix some of the decision variables in M_0 allowed us to increase the number of solved instances and achieve greater computational efficiency.

With the one-phase approach, instead, routing decisions are considered jointly with the scheduling and assignment ones, within the same model (M_0^{routing}). Such a model is obtained by adding routing constraints to the baseline one (and a few other minor changes, see Section 4.4). The solution returned by M_0^{routing} provides a benchmark for appraising the quality of the solutions of the other models and for assessing the advantages in terms of computational performance associated with the two-phase approach.

4.1. Baseline model

Hereafter, we report the constraints shared by all the deterministic models used in the experimentation.

$$\sum_{(r,d') \in A^p} f_{prd'} = 1 \ \forall p \in P \tag{1}$$

$$\sum_{(d',d) \in A^p} f_{pd'd} - \sum_{(d,d') \in A^p} f_{pdd'} = 0 \ \forall p \in P, \ \forall d \in D^p \tag{2}$$

Table 3
Variables.

Symbol	Type	Description	Domain
$f_{pdd'}$	Binary	1 if patient p receives the treatment on day d' after receiving treatment on day d, 0 otherwise	$\forall p \in P, \forall (d,d') \in A^p$
y_{pdos}	Binary	1 if patient p receives the treatment on day d from operator o in setting s, 0 otherwise	$\forall p \in P, \forall d \in D^p, \forall o \in O,$ $\forall s \in S^p$
k_{dos}	Binary	1 if operator o works on day d in setting s, 0 otherwise	$\forall d \in D, \forall o \in O, \forall s \in S$
z_{po}	Binary	1 if operator o is assigned to patient p, 0 otherwise	$\forall p \in P, \forall o \in O$
x_d	Binary	1 if the center is open on day d, 0 otherwise	$\forall d \in D$
v_p	Binary	1 if patient $p \in P\backslash P^c$ is assigned to the home care setting, 0 otherwise	$\forall p \in P\backslash P^c$
q_{pd}	Binary	1 if patient $p \in P^c$ is scheduled on day d (in the auxiliary model)	$\forall p \in P^c, \forall d \in D$
g_{doij}	Binary	1 if on day d operator o visits node j after visiting node i, 0 otherwise (in the routing model)	$\forall d \in D^i \cap D^j$ $\forall o \in O$ $\forall i \in P\backslash P^c \cup \{r\}$, $\forall j \in P\backslash P^c \cup \{r\}$
m_{dop}	Non Negative Reals	The position of patient p in the tour of operator o on day d (in the routing model)	$\forall d \in D$ $\forall o \in O$ $\forall p \in P\backslash P^c$
y^e_{pdoc}	Binary	1 if in scenario e patient p on day d is treated at the center by operator o to manage the adverse event, 0 otherwise (in the stochastic model)	$\forall e \in E, \forall p \in P\backslash P^c, \forall d \in D^p,$ $\forall o \in \overline{O}$
k^e_{dos}	Binary	1 if in scenario e operator o works on day d in setting s, 0 otherwise, (in the stochastic model)	$\forall e \in E, \forall d \in D, \forall o \in O, \forall s \in S$
t^e_{do}	Non Negative Reals	Overtime made by operator o on day d in scenario e (in the stochastic model)	$\forall e \in E, \forall d \in D, \forall o \in O$
a^e_d	Binary	1 if in scenario e on day d it is necessary to activate the operator $\bar{o}$, 0 otherwise (in the stochastic model)	$\forall e \in E, \forall d \in D$

$$\sum_{(d,t) \in A^p} f_{pdt} = 1 \ \forall p \in P \quad (3)$$

$$\sum_{(d',d) \in A^p} f_{pd'd} = \sum_{s \in S^p} \sum_{o \in O} y_{pdos} \ \forall p \in P, \ \forall d \in D^p \quad (4)$$

$$y_{pdoh} \le v_p \ \forall p \in P\backslash P^c, \ \forall d \in D, \ \forall o \in O \quad (5)$$

$$y_{pdoc} \le 1 - v_p \ \forall p \in P\backslash P^c, \ \forall d \in D, \ \forall o \in O \quad (6)$$

$$\sum_{d \in U^p} \sum_{o \in O} y_{pdoh} \le \sigma_p \ \forall p \in P\backslash P^c \quad (7)$$

$$\sum_{d \in U^p} \sum_{o \in O} y_{pdoc} = 0 \ \forall p \in P \quad (8)$$

$$k_{dos} \ge y_{pdos} \forall p \in P, \ \forall d \in D^p, \ \forall o \in O, \ \forall s \in S^p \quad (9)$$

$$\sum_{s \in S} k_{dos} \le 1 \ \forall d \in D, \ \forall o \in O \quad (10)$$

$$\sum_{p \in P\backslash P^c \ s.t. \ d \in D^p} (\delta_p + \overline{\varphi}_p) y_{pdoh} \le (\alpha_o - \overline{\varphi}_c) k_{doh} \ \forall d \in D, \ \forall o \in O \quad (11)$$

$$\sum_{p \in P \ s.t. \ d \in D^p} \delta_p y_{pdoc} \le \alpha_o k_{doc} \ \ \forall d \in D, \ \forall o \in O \quad (12)$$

$$z_{po} \ge y_{pdos} \ \forall p \in P, \ \forall d \in D^p, \ \forall o \in O, \ \forall s \in S^p \quad (13)$$

$$\sum_{o \in O} z_{po} \le \omega_p \ \forall p \ \epsilon \ P \quad (14)$$

$$x_d \ge k_{doc} \ \forall d \in D, \forall o \in O \quad (15)$$

$$\sum_{d \in w} \sum_{s \in S} k_{dos} \le \beta_o \ \forall w \in W, \forall o \in O \quad (16)$$

$$\sum_{o \in O} k_{doc} \le \theta \ \forall d \in D \quad (17)$$

$$\sum_{o \in O} k_{doh} \le \rho \ \forall d \in D \quad (18)$$

$$\sum_{d \in D^p} \sum_{o \in O} \sum_{s \in S^p} y_{pdos} \ge \psi_p \ \forall p \in P \quad (19)$$

The first three sets of constraints (Constraints (*1*), (*2*), and (*3*)) assure flow conservation. Specifically, they have a multicommodity structure where a commodity is associated with each patient p. For each patient p, they define a path that starts at the root node r (Constraints (*1*)), enters the terminal node t (Constraints (*3*)), and flows through intermediate nodes corresponding to the days on which patient p receives treatments (Constraints (*2*)). Constraints (*4*) link the variables $f_{pdd'}$ and y_{pdos}; they guarantee that if patient p is treated on day d, the treatment is given by exactly one operator active in a setting that is feasible to patient p. Constraints (*5*) and (*6*) ensure that each patient p is assigned to only one setting over the entire planning horizon – if they are assigned to the home care setting (Constraints (*5*)) on a certain day d, they will remain associated with it in D, and the same applies to the center. Constraints (*7*) and (*8*) control the maximum number of times patient preferences can be violated. Patients assigned to the home care setting can receive the service on an undesirable day a maximum of σ_p times (Constraints (*7*)), while patients assigned to the center setting cannot be treated on an undesirable day (Constraints (*8*)). Note that Constraints (*8*) fix variables to zero. More correctly, this restriction should be handled at the variable's domain level by excluding the existence of a variable y_{pdoc} relating to the center setting and to a day disliked by p. However, for greater readability of the model and not having to distinguish the domain of the y each time depending on whether they refer to one setting rather than the other, we preferred to write Constraints (*8*) explicitly. Constraints (*9*) ensure that if patient p receives treatment on day d by operator o in setting s, then that operator must be active on that day and in that setting. Constraints (*10*) guarantee that each operator cannot work in both home care and center settings on the same day. Constraints (*11*) and (*12*) control that operators' workload cannot exceed the shift duration α_o, respectively for operators working in the home care setting and at the center. Specifically, for home care operators, the workload is given by the sum of the service time for the treated patients, the mean traveling time to reach them, and the mean traveling time to get back to the center. For operators working at the center, only service times are considered. Constraints (*13*) link the variables z_{po} with y_{pdos}, imposing that if patient p on a given day is treated by the operator o then the patient-operator assignment variable z_{po} is set to 1. Constraints (*14*) impose the continuity of care for both settings: according to them a

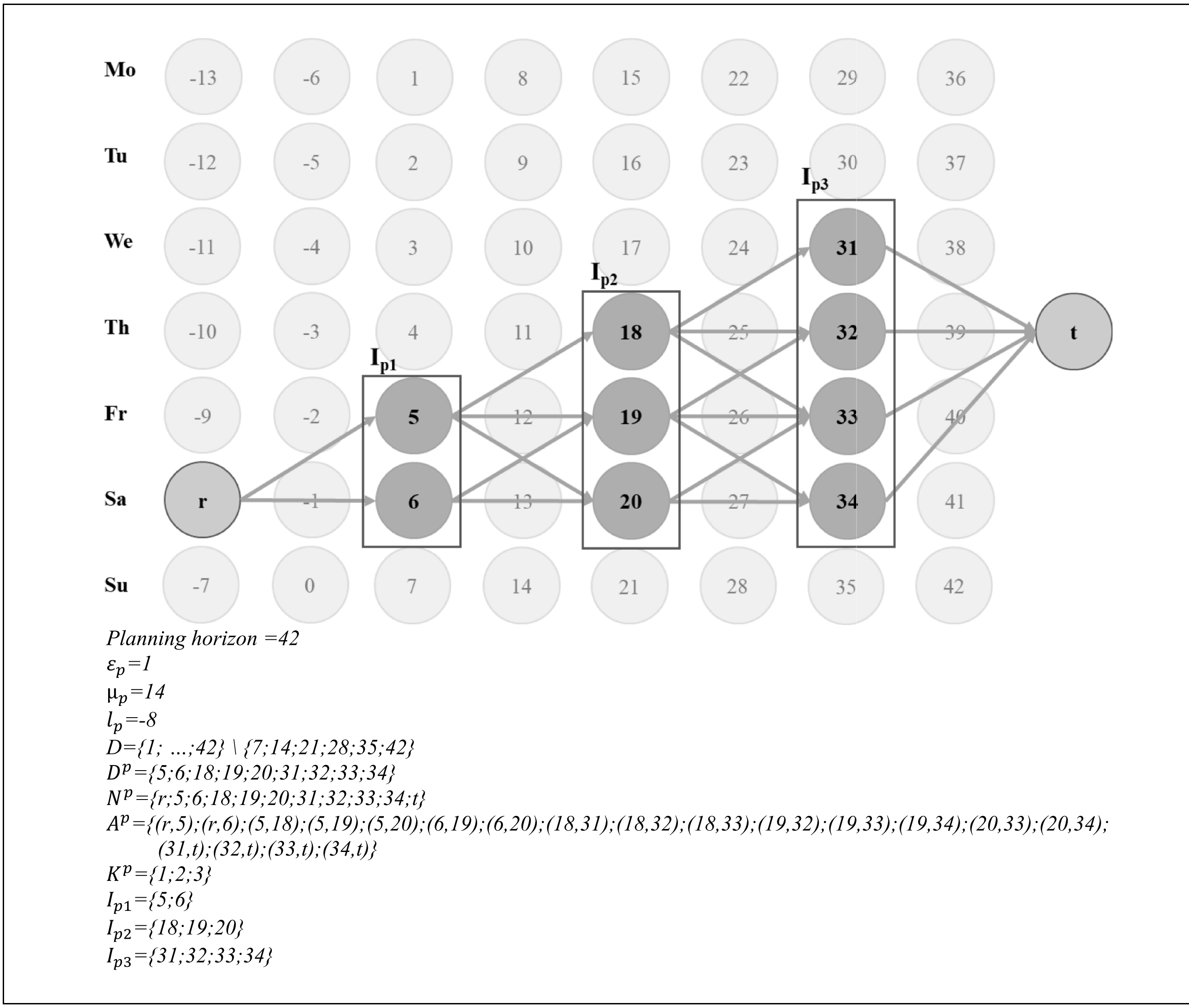

Fig. 1. Example of graph.

maximum of ω_p operators can be assigned to patient p during the planning horizon. Constraints (*15*) book the center if at least one operator is working on that day in the center setting; vice versa, if the center has not been booked, no operator can work there. Constraints (*16*) impose that each operator works at most β_o days per week. Constraints (*17*) and (*18*) are the capacity constraints respectively at the center and in the home care setting. Specifically, since there are θ stations at the center and a maximum of one operator per station is allowed, at most θ operators will be active at the center per day. Similarly, Constraints (*18*) assure that the maximum number of operators active in the home care setting per day is at most ρ, i.e., the number of available cars (a maximum of one operator per car). Constraints (*19*) impose that, for each patient, the number of treatments given in the entire planning horizon complies with the treatment frequency defined in the care plan of patients. In fact, if these constraints were not present, the tolerance of the time between two successive treatments could lead to an insufficient number of treatments. The minimum number of treatments can be computed for each patient, as described in Table 2, considering the last treatment time. The baseline model also includes valid inequalities (27) and (28) that will be described in Section 4.2.

Eq. (20) reports OF_1, while Eq. (21) reports OF_2. OF_1 minimizes the total cost for the provider calculated as the sum of the center cost (first term), the operator cost (second term), and the provider travel cost (third and fourth terms). OF_2 minimizes the distance traveled by patients treated at the center.

$$OF_1 = \min \sum_{d \in D} \lambda x_d + \sum_{d \in D} \sum_{o \in O} \sum_{s \in S} \eta k_{dos} + \sum_{p \in P \setminus P^c} \sum_{d \in D^p} \sum_{o \in O} \pi \, \overline{\gamma_p} y_{pdoh} + \sum_{d \in D} \sum_{o \in O} \pi \, \overline{\gamma_c} k_{doh} \tag{20}$$

$$OF_2 = \min \sum_{p \in P} \sum_{d \in D} \sum_{o \in O} \left(\gamma_{pc} + \gamma_{cp}\right)^* y_{pdoc} \tag{21}$$

As already pointed out, to prevent the use of OF_2 from leading to an indiscriminate increase in provider costs, when OF_2 is used, we constrain these costs to be less than or equal to Δ percent of the cost (Ω) of the optimal solution obtained with OF_1. This is done by adding Constraint (*22*) to the Constraints (*1*)-(*19*) characterizing the first model.

$$\sum_{d \in D} \lambda x_d + \sum_{d \in D} \sum_{o \in O} \sum_{s \in S} \eta k_{dos} + \sum_{p \in P \setminus P^c} \sum_{d \in D^p} \sum_{o \in O} \pi \overline{\gamma_p} y_{pdoh} + \sum_{d \in D} \sum_{o \in O} \pi \overline{\gamma_c} k_{doh} \le (1+\Delta)^* \Omega \quad (22)$$

It is worth observing that in OF_1 we approximate the distances between a given patient p and all the other patients and between the patient and the center c with $\overline{\gamma_p}$ and $\overline{\gamma_c}$, respectively. Similarly, in Constraints (*11*), the travel times are approximated with $\overline{\varphi}_p$ and $\overline{\varphi}_c$. The actual travel distance and time for each operator are established in the second phase when the actual operator route is determined using a TSP model. The effect of this approximation will be evaluated in Section 7.4.

4.2. Auxiliary model and valid inequalities

With the auxiliary model, we address the problem of establishing the minimum number of days on which to book the center (variables x_d in Table 3) to schedule all the patients that necessarily need to be scheduled at the center (P^c). The model has a set covering-like structure, and it is formulated as follows.

$$OF_0 = \min \sum_{d \in D} x_d \quad (23)$$

$$\sum_{d \in I_{pk}} q_{pd} \ge 1 \ \forall p \in P^c, \ \forall k \in K^p \quad (24)$$

$$\mu_p - \varepsilon_p \le \sum_{d \in I_{p(k+1)}} d q_{pd} - \sum_{d \in I_{pk}} d q_{pd} \le \mu_p + \varepsilon_p \ \forall p \in P^c, \ \forall k < |K^p| \quad (25)$$

$$\sum_{p \in P^c \ s.t. \ d \in D^p} \delta_p q_{pd} \le \theta \ \alpha_o x_d \ \forall d \in D \quad (26)$$

The objective function OF_0 (Eq. (23)) minimizes the number of days the center is booked. Constraints (*24*) impose that each patient receives the k^{th} treatment in the proper interval I_{pk}. Constraints (*25*) ensure that two consecutive treatments are correctly sequenced in time. Specifically, the distance between two consecutive treatments must be at least $\mu_p - \varepsilon_p$ days and at most $\mu_p + \varepsilon_p$ days. Constraints (*26*) guarantee that the total duration of all treatments scheduled on day $d \in D$ does not exceed the cumulative daily capacity of the center which is given by $\theta \times \alpha_o$ when the center is open ($x_d = 1$) and zero otherwise (here we assume for simplicity that the duration of the shifts is the same for all the operators).

From the solution of the auxiliary model, we can derive the valid inequality (*27*). In fact, the number of days in which the center is booked in the auxiliary model is a lower bound for the number of days in which the center will be booked when the whole set of patients is analyzed.

Let $\overline{x}_d$ be the optimal solution of the auxiliary model. Then, the following Constraint holds.

$$\sum_{d \in D} x_d \ge \sum_{d \in D} \overline{x}_d \quad (27)$$

Another valid inequality can be obtained by observing that a trivial lower bound for the minimum number of working days required to cover the total request can be computed by dividing the total service time by the longest shift duration as follows.

$$\sum_{d \in D} \sum_{o \in O} \sum_{s \in S} k_{dos} \ge \left\lceil \frac{\left(\sum_{p \in P} \delta_p \psi_p\right)}{max_{o \in O} \{\alpha_o\}} \right\rceil \quad (28)$$

In our experimentation, Constraints (*27*) and (*28*) are included in all model variants to improve their computational performance. The effect of this inclusion are presented in Section 7.3.

4.3. Matheuristics

To increase the number of solved instances and achieve greater computational efficiency, we have also devised two matheuristics. It is important to note that in this context, the term "matheuristic" is not employed to signify a methodology that combines an optimization model with a heuristic (such as local search, Tabu Search, Simulated Annealing, etc.). Instead, it identifies an approach to obtain sub-optimal solutions in a computationally less demanding way by fixing the value of certain decision variables [54,40]. Our matheuristics are characterized by a different level of flexibility depending on which decisions are retained in the original problem. Both of them are based on the solution of AUX.

The first matheuristic requires the center to be booked on the days established by the optimal solution of the auxiliary problem (see Constraints (*29*)).

$$x_d \ge \overline{x}_d \ \forall d \in D \quad (29)$$

Thus, the first matheuristic consists of a model characterized by the Constraints (*1*)-(*19*), (*27*)-(*29*), and OF_1.

The second matheuristic, in addition to retaining the decision on when to book the center (Constraints (*29*)), also assigns the patients in P^c to days d according to the optimal solution of the auxiliary problem (Constraints (*30*)). In such constraints, $\overline{q}_{pd}$ represents the value of the variables q_{pd} in the optimal auxiliary model's solution.

$$\sum_{o \in O} y_{pdoc} \ge \overline{q}_{pd} \ \forall p \in P^c, \ \forall d \in D^p \quad (30)$$

Thus, the second matheuristic consists of a model characterized by the Constraints (*1*)-(*19*), (*27*)-(*30*), and OF_1.

Note that Constraints (*26*) of the auxiliary model are indeed a relaxation of Constraints (*12*) which assure that, separately for each operator, the time spent treating patients does not exceed the duration of the shift. Thus, imposing patients' treatment according to $\overline{q}_{pd}$, may make the problem unfeasible. To prevent this, the feasibility of the auxiliary model's solution is checked, and for each day when Constraints (*12*) are violated, the value of $\overline{q}_{pd}$ corresponding to the patient p with the longest treatment is set to zero in Constraints (*30*) until the solution becomes feasible.

4.4. Model with embedded routing

To embed the routing decisions in the baseline model, we added Constraints (*31*)-(*34*) and Constraints (*36*)-(*38*) to the baseline model, substituted Constraints (*11*) with Constraints (*35*), and changed OF_1 from (*20*) to (*39*).

$$\sum_{p \in P^d} g_{dorp} = k_{doh} \ \forall d \in D, \forall o \in O \quad (31)$$

$$\sum_{p' \in P^d} g_{dop'p} - \sum_{p' \in P^d} g_{dopp'} = 0 \ \forall d \in D, \forall o \in O, \forall p \in P^d \quad (32)$$

$$\sum_{p \in P^d} g_{dopr} = k_{doh} \ \forall d \in D, \forall o \in O \quad (33)$$

$$\sum_{p' \in P^d} g_{dop'p} = y_{pdoh} \ \forall p \in P \setminus P^c, \forall d \in D, \forall o \in O \quad (34)$$

$$\sum_{\substack{p',p \in P \setminus P^c \cup \{r\} \\ s.t. \ d \in D^p \cap D^{p'}}} \left(\delta_p + \varphi_{p'p}\right) g_{dop'p} \le \alpha_o k_{doh} \ \forall d \in D, \ \forall o \in O \quad (35)$$

$$(assuming \ \delta_r = 0)$$

$$g_{dopp'} + g_{dop'p} \le 1 \ \forall p, p' \in P \setminus P^c, \forall d \in D, \forall o \in O \quad (36)$$

$$m_{dor} = 0 \; \forall \, d \in D, \forall \, o \in O \tag{37}$$

$$m_{dop'} \geq 1 + m_{dop} - |P^d| \left(1 - g_{dopp'}\right) \forall \, p, p' \in P \backslash P^c, \forall \, d \in D, \forall \, o \in O \tag{38}$$

$$OF_1^{routing} = \min \sum_{d \in D} \lambda x_d + \sum_{d \in D} \sum_{o \in O} \sum_{s \in S} \eta k_{dos} + \sum_{p',p \in P \backslash P^c \cup \{r\}} \sum_{d \in D^p \cap D^{p'}} \sum_{o \in O} \pi \gamma_{ij} \, g_{dop'p} \tag{39}$$

The first three sets of constraints (Constraints (*31*), (*32*), and (*33*)) assure flow conservation. For each operator o and each day d, they define a tour that starts and ends at the dummy node r (Constraints (*31*) and (*33*)) flowing through intermediate nodes corresponding to the houses of patients that have been assigned to operator o in day d in setting h (Constraints (*32*)) if the operator is active on that day in that setting. Constraints (*34*) link the variables $g_{dopp'}$ and y_{pdoh}; they guarantee that if patient p is treated on day d by operator o in setting h, on that day the operator o in setting h is following a tour that passes through patient p. Constraints (*35*) control that operators' workload cannot exceed the shift duration α_o for operators working in setting h. Specifically, the workload is given by the sum of the service time for the treated patients and the total (exact) traveling time to make the tour (time to move from the dummy node r to the first patient served in day d, time to reach all the patients in the tour of the operator o on day d, and travel time to move from the last patient in the tour of operator o on day d to the dummy node r). Constraints (*36*)-(*38*) manage subtour elimination. Specifically, Constraints (36) break two-node cycles and guarantee that if patients p and p' belong to the tour of operator o on day d, either p precedes p' or p' precedes p. These constraints are used to tight the classical MTZ-constraints in which nodes belonging to a tour are labeled with their position in the tour (variables m_{dop}): dummy node r, which is the first node in the tour, has a label set to zero (Constraints (37)), while (Constraints (38)) the label $m_{dop'}$ of node p' is greater than the label $m_{dop}$of node p when the operator travels from p to p' ($g_{dopp'} = 1$). Parameter $|P^d|$ is used to make Constraints (38) redundant when $g_{dopp'} = 0$.

$OF_1^{routing}$ (*39*) minimizes the total cost for the provider calculated as the sum of the center cost (first term), the operator cost (second term), and the provider (exact) travel cost (third term). The first and second terms are the same of OF_1, while the third term is calculated exactly in $OF_1^{routing}$considering the routing followed by operators.

5. Stochastic model

In the stochastic model we consider a number $|E|$ of different sets of adverse events. Each of these set is identified by the letter e and it is characterized by a probability of occurrence ξ_e. Across the sets e patients experiencing an adverse event and the day of occurrence of such an event varies randomly. However, the number of affected patients ($\nu \times |P|$) is the same for all sets. Table 4 reports an example with ν=10 %, $|P|$=30 and $|E|$=*5*. Each row in the table represents a set of adverse events involving three patients. The probability of occurrence of each set is ξ_e=0.2. As an example, when $e = 1$, the three affected patients are 1, 20, and 29, and for them, the adverse event occurs respectively on days 25, 74, and 86.

Table 4
Example of a set of adverse events with $|E|$=5.

ξ_e	e	(patient, day)
0.2	1	(1,25); (20,74); (29,86)
0.2	2	(18,36); (15,48); (28,6)
0.2	3	(21,28); (10,58); (4,4)
0.2	4	(26,68); (8,82); (3,51)
0.2	5	(5,72); (6,57); (19,16)

In the stochastic model, two types of decisions are kept constant across scenarios: the days on which the center is open and the days on which visits are scheduled. Adverse events do not affect patients assigned to the center. Conversely, if a patient is assigned to home care and has an adverse event on day d, all the subsequent treatments, i.e., those planned in the following days $\{d + 1, \ldots, T\}$, will necessarily be rescheduled at the center. In that case, two situations may occur. If the patient's treatment is scheduled on days on which the center was not booked, the center will have to be open with extra resources, i.e., an additional operator ($\overline{o}$) is activated upon request, and the activation cost considers the cost of both the facility and the additional operator. If the patient's treatment is scheduled when the center was already booked, the patient will be assigned to one of the operators already active at the center for that day, with possible overtime costs. The activation of the operator $\overline{o}$ incurs a cost (χ) that is higher than that of operators in set O. The hourly cost of operator overtime (ζ) is greater than their ordinary hourly cost.

The objective of the stochastic model is to minimize the expected provider costs ($OF_1^{stochastic}$, provider-oriented) by considering a set of scenarios weighted by their probability of occurring.

$$\sum_{(r,d') \in A^p} f_{prd'} = 1 \quad \forall \, p \in P \tag{40}$$

$$\sum_{(d',d) \in A^p} f_{pd'd} - \sum_{(d,d') \in A^p} f_{pdd'} = 0 \; \forall \, p \in P, \; \forall \, d \in D^p \tag{41}$$

$$\sum_{(d,t) \in A^p} f_{pdt} = 1 \; \forall \, p \in P \tag{42}$$

$$\sum_{(d',d) \in A^p} f_{pd'd} = \sum_{o \in O} \sum_{s \in S^p} \left(1 - u_{pd}^e\right) y_{pdos} + \sum_{o \in \overline{O}} u_{pd}^e \, y_{pdoc}^e \; \forall \, e \in E, \; \forall \, p \in P, \; \forall \, d \in D^p \tag{43}$$

$$y_{pdoh} \leq v_p \; \forall \, p \in P \backslash P^c, \; \forall \, d \in D, \; \forall \, o \in O \tag{44}$$

$$y_{pdoc} \leq 1 - v_p \; \forall \, p \in P \backslash P^c, \; \forall \, d \in D, \; \forall \, o \in O \tag{45}$$

$$\sum_{d \in U^p} \sum_{o \in O} y_{pdoh} \leq \sigma_p \; \forall \, p \in P \backslash P^c \tag{46}$$

$$\sum_{d \in U^p} \sum_{o \in O} y_{pdoc} = 0 \; \forall \, p \in P \tag{47}$$

$$k_{doh}^e \geq \left(1 - u_{pd}^e\right) y_{pdoh} \; \forall \, e \in E, \forall \, p \in P \backslash P^c, \forall \, d \in D, \forall \, o \in O \tag{48}$$

$$k_{doc}^e \geq \left(1 - u_{pd}^e\right) y_{pdoc} + u_{pd}^e y_{pdoc}^e \; \forall \, e \in E, \forall \, p \in P, \forall \, d \in D, \forall \, o \in O \tag{49}$$

$$k_{doh}^e + k_{doc}^e \leq 1 \; \forall \, e \in E, \forall \, d \in D, \forall \, o \in O \tag{50}$$

$$\sum_{p \in P \backslash P^c \text{ s.t. } d \in D^p} (\delta_p + \overline{\varphi}_p) \left(1 - u_{pd}^e\right) y_{pdoh} \leq (\alpha_o - \overline{\varphi}_c) k_{doh}^e \quad \forall \, e \in E, \forall \, d \in D, \; \forall \, o \in O \tag{51}$$

$$\sum_{p \in P \text{ s.t. } d \in D^p} \delta_p \left[\left(1 - u_{pd}^e\right) y_{pdoc} + u_{pd}^e y_{pdoc}^e\right] \leq \alpha_o k_{doc}^e + t_{do}^e \quad \forall \, e \in E, \; \forall \, d \in D, \; \forall \, o \in O \tag{52}$$

$$z_{po} \geq y_{pdos} \forall \, p \in P, \; \forall \, d \in D^p, \; \forall \, o \in O, \; \forall \, s \in S^p \tag{53}$$

$$\sum_{o \in O} z_{po} \leq \omega_p \; \forall \, p \in P \tag{54}$$

$$x_d \geq k^e_{doc} \; \forall e \in E, \forall d \in D, \forall o \in O \tag{55}$$

$$\sum_{d \in w} \sum_{s \in S} k^e_{dos} \leq \beta_o \; \forall e \in E, \forall w \in W, \forall o \in O \tag{56}$$

$$\sum_{o \in O} k^e_{doc} \leq \theta \; \forall e \in E, \forall d \in D \tag{57}$$

$$\sum_{o \in O} k^e_{doh} \leq \rho \; \forall e \in E, \forall d \in D \tag{58}$$

$$\sum_{d \in D^p} \sum_{o \in O} \sum_{s \in S^p} y_{pdos} \geq \psi_p \; \forall p \in P^c \tag{59}$$

$$\sum_{d \in D^p} \sum_{o \in O} \sum_{s \in S^p} \left[\left(1 - u^e_{pd}\right) y_{pdos} + \left(u^e_{pd}\right) y^e_{pdoc} \right] + \sum_{d \in D^p} u^e_{pd} y^e_{pd\bar{o}c} \geq \psi_p \; \forall e \in E, \forall p \in P \backslash P^c \tag{60}$$

$$y^e_{pd\bar{o}c} \leq a^e_d \; \forall e \in E, \; \forall p \in P, \; \forall d \in D^p \tag{61}$$

$$y^e_{pdoc} = 0 \; \forall e \in E, \forall p \in P^c, \forall o \in O, \forall d \in D \tag{62}$$

$$OF^{stochastic}_1 = \min \sum_{d \in D} \lambda x_d + \sum_{e \in E} \xi_e \left(\sum_{d \in D} \sum_{o \in O} \sum_{s \in S} \eta k^e_{dos} + \sum_{p \in P \backslash P^c} \sum_{d \in D^p} \sum_{o \in O} \pi \overline{\gamma_p} \left(1 - u^e_{pd}\right) y_{pdoh} + \sum_{d \in D} \sum_{o \in O} \pi \overline{\gamma_c} k^e_{doh} + \sum_{d \in D} \chi a^e_d + \sum_{d \in D} \sum_{o \in O} \zeta t^e_{do} \right) \tag{63}$$

Constraints (*40*)-(*42*) assure flow conservation on the $f_{pdd'}$ variables, and as already noted, do not depend on the scenario. Constraints (*43*) link the variables $f_{pdd'}$, y_{pdos}, and y^e_{pdoc}; they guarantee that if patient *p* is treated on day *d*, the treatment is given by exactly one operator active in a setting that is feasible to patient *p* if the patient did not have an adverse event until *d*, otherwise, the treatment is given at the center by one operator active in the setting *c* that day or by the additional operator $\bar{o}$. Constraints (*44*) and (*45*) ensure that patients are assigned to only one setting over the entire planning horizon if they are not affected by adverse events. Constraints (*46*) and (*47*) control the maximum number of times patient preferences can be violated. Constraints (*48*), scenario-wise, ensure that if patient *p*, not yet affected by an adverse event, receives treatment on day *d* by operator *o* in setting *h*, then that operator must be active on that day in that setting and in that scenario. Constraints (*49*), scenario-wise, ensure that operators at the center are activated either to treat patients not yet affected by an adverse event or patients who have been assigned to the center after an adverse event. Constraints (*50*), scenario-wise, ensure that an operator cannot work simultaneously in the home and center settings on the same day *d*. Constraints (*51*), scenario-wise, control that operators' workload cannot exceed the shift duration α_o for operators working in the home care setting. Constraints (*52*), scenario-wise, control operators' workload for operators working at the center. In Constrains (*51*), the patients considered are those not affected by an adverse event, while in Constraints (*52*), both affected and not affected patients are considered according to the day on which the adverse event involving them possibly occurred. In Constraints (*52*), we accept an overtime (t^e_{do}) in the workload of center operators to deal with the consequences of adverse events. Constraints (*53*) link the variables z_{po} with y_{pdos}, imposing that if patient *p* on a given day is treated by the operator *o* then the patient-operator assignment variable z_{po} is set to 1. Constraints (*54*) impose the continuity of care for both settings. Constraints (*55*) book the center if at least one operator is working on that day in the center setting; vice versa, if the center has not been booked, no operator can work there. As already observed, variables x_d do not depend on scenarios. Constraints (*56*) impose that, in each scenario, each operator works at most β_o days per week. Constraints (*57*) and (*58*) are the capacity constraints respectively at the center and in the home care setting, again for each scenario. Constraints (*59*) and (*60*), respectively for not flexible and flexible patients, impose that, for each patient, the number of treatments given in the entire planning horizon complies with the treatment frequency defined in the care plan of patients. Specifically, Constraints (*60*) impose that, for flexible patients, the total number of visits is obtained by also considering the ones made after the adverse event. Constraints (*61*) fix that in each scenario *e* and on each day *d* if a patient received treatment by the operator $\bar{o}$, the extra operator $\bar{o}$ has to be activated. Constraints (*60*) control that variable y^e_{pdoc} is set to zero for all patients that have to be treated at the center ($\forall p \in P^c$). In the implementation of the model such constraints are implicitly considered in the variable domain and are presented here in this form to avoid differentiating the constraints according to the patient considered. Eq. (63) reports the objective function $OF^{stochastic}_1$. It minimizes the expected total cost for the provider calculated as the sum of the center cost (first term), the operator cost (second term), the provider travel cost (third and fourth terms), the cost of the additional operator $\bar{o}$ (fifth term), and the cost of overtime at the center (sixth term). All costs, except center costs, are calculated separately for each scenario and weighted according to its probability of occurrence.

6. Experimental campaign

6.1. Objectives

The objectives of our experimental campaign are fivefold: (i) quantifying the benefits that it is possible to achieve in different operating conditions by switching from a CBC model to an FC one; (ii) determining the operating conditions that make the use of one of the proposed models preferable to the others; (iii) assessing the error that originates from using approximated travel distances; (iv) comparing the results obtained with OF_1 and OF_2; (v) assess how adverse events may affect the solution.

To obtain results as generalizable as possible, we generated a wide set of random instances that are described in the next section. The optimization models were coded in Python-Pyomo and solved using CPLEX 20.1 on a PC equipped with a CPU Intel i7–4930 K @ 3.40 GHz and 32 GB of RAM.

6.2. Model testing

In our experimental campaign, we ran several variants of the model obtained as described in Table 5. For benchmarking purposes, the baseline model was also run assuming that all patients could be scheduled only at the center (see M_3).

6.3. Instances creation

Using the free and open global address collection *open address* (https://openaddresses.io/), we randomly sampled a set of 50 addresses in a medium Italian city (Florence, Area 102.4 km^2, Population (2021) 361,619) and assumed that these were the home addresses of 50 patients needing a specific treatment that can be administered both at home or at a center. Then, using the *open route* web service (https://openrouteservice.org/), we calculate the two matrices Γ and Φ (Table 2), indicating, respectively, the travel distance and travel time between each pair of patients and between each patient and a known hospital hosting several outpatient clinics. These matrices were calculated considering the actual road route to be followed; therefore, they are not symmetrical. Each patient, then, was assigned the parameter l_p randomly sampling from [-μ_p+1,0], the parameter U^p randomly considering undesirable either the odd days of the week or the even

Table 5
Description of the models included in the experimental campaign.

Model ID	Obj. fun.	Constraints	Description
M_0	(20)	(1)-(19), (27), (28)	Baseline model with OF_1
M_1	(20)	(1)-(19), (27), (28) and (29)	Matheuristic 1 with OF_1
M_2	(20)	(1)-(19), (27), (28) and (29, 30)	Matheuristic 2 with OF_1
M_3	(20)	(1)-(19), (27)-(28) and $P^c \equiv P$	Baseline model, where it is assumed that all patients should be scheduled at the center, with OF_1
$M_0^{routing}$	(39)	(1)-(10), (12)-(19), (27), (28), (31)-(38)	Baseline model with OF_1 and routing constraints
M_4	(21)	(1)-(19), (27), (28) and (22)	Baseline model with OF_2
AUX	(23)	(24)-(26)	Auxiliary set-covering-like model
M_E^{stoc}	(63)	(40)-(62)	Stochastic model based on $\|E\|$ set of adverse events

Table 6
Parameters not varying across instances.

Parameter	Value
η	100 €
π	0.6 €/km
μ_p	14 days
ω_p	2
σ_p	2
Δ	5 %
α_o	360 min
β_o	5 days
T	90 days

Table 7
Parameters differing between deterministic and stochastic models.

Parameter	Value (for deterministic models)	Value (for stochastic model)
$\|P\|$	50	30
$\|O\|$	4	2
θ	3	2
ρ	3	2

ones. All these parameters were held fixed across instances. The value of the other models' parameters held fixed in our experimentation are reported in Table 6, while Table 7 reports the parameters differing between the instances used for (all) the deterministic models and the stochastic one (for which to reduce the computational burden we used a subset of 30 patients randomly sampled from the mentioned 50 ones). For the sake of simplicity, we considered μ_p to be fixed across patients, and hence it will be referred to as μ in the following. These values have been inspired by the real case of an Italian provider who supplies infusion therapy to patients with Fabry disease. Such a disease is relentlessly progressive and inevitably disabling [55]. Patients with Fabry disease require infusion treatment once every 14 days [56]. For these patients, home care, when feasible, can substantially enhance the quality of life [57], bolster treatment adherence, and mitigate infection risks [58]. In addition, due to the challenges posed by the Fabry disease to maintaining a regular lifestyle, it is of utmost importance to schedule home treatment in a way that takes into account the patient's preferences and ensures continuity of care [59,60].

To generate instances representing a wide set of different operating conditions, we used three *relative* parameters tying together the main problem features. These relative parameters are Treatment Time Multiplier (TTM), Center Cost Multiplier (CCM), and Center-only Patients Percentage (CPP).

TTM ties together travel time and treatment time. It was used to represent both situations in which the duration of the treatment can be much higher than the average time taken to travel to the patient as well as situations in which this difference is smaller. The patient treatment time was thus calculated as $\delta_p = \overline{\overline{\varphi}}$ (TTM+*rnd()*), where *rnd() is* a random integer $\in$ [−1,0,1]. Since the expected value of *rnd()* is 0, δ_p is, on average, TTM times $\overline{\overline{\varphi}}$.

CCM ties together the daily cost to book the center for patients needing a certain treatment and the daily cost of an operator able to administer that treatment. The daily cost of the center λ was thus calculated as λ =CCM $\times$ η and the values of CCM were selected to represent situations where the relative magnitude of these costs varies over a wide range.

Table 8
Parameters varying across instances for the deterministic models.

Parameter	Values used in the experimental campaign	Values corresponding to the real case
TTM	{2, 3.5, 5}	3.5
CCM	{1, 3, 10}	3
CPP	{10, 20}	20
ε	{0, 1, 2}	1

CPP represents the percentage of patients who must be treated at the center.

In addition to these relative parameters, we also tested different values of the tolerance (ε_p) to represent both situations in which the time between two consecutive treatments is fixed (ε_p=0) and equal to μ_p and situations in which the treatment protocol for the disease is not so rigid and allows the interval between two consecutive treatments to vary between [μ_p - ε_p, $\mu_p + \varepsilon_p$]. For the sake of simplicity, we considered ε_p to be fixed across patients, and hence it will be referred to as ε in the following.

The values of the parameters that vary across instances for the deterministic models are reported in Table 8 which also reports the value corresponding to the real case inspiring this work.

Combining these four parameters we obtained 54 different instances representing a wide set of heterogeneous operating conditions. For each instance, we tested the models M_0, M_1, M_2, M_3, and $M_0^{routing}$, obtaining 270 solutions (Section 7.1). Results relevant to these scenarios are discussed in the next section. To compare OF_1 and OF_2, we run model M_4 holding ε = 1, thereby obtaining an additional 18 solutions (Section 7.2). Finally, to assess the effect of the valid inequalities on M_0, we ran other 270 instances (see Section 7.3). All the deterministic models have been tested setting a gap limit of 1 % and a time limit of 1 hour. To test the stochastic model, we fixed the model parameters as reported in Table 9. Across instances, the number of affected patients does not vary and it is equal to ν=10 % of the total number of patients as suggested by the literature [61,62] and confirmed by the healthcare professional who inspired this study. The *hourly overtime cost* (ζ) was set as twice the operators' hourly cost (η/α_o), the operator $\overline{o}$ activation cost (χ) was set as

Table 9
Parameters in the stochastic model.

Parameter	Values
TTM	3.5
CCM	10, 1
CPP	20
ν	10 %
ε	1
$\|E\|$	{3, 5, 7, 10}
ξ_e	$1/\|E\|$
ζ	$2 \times \eta/\alpha_o$
χ	$2\eta \times$ (1+CCM))

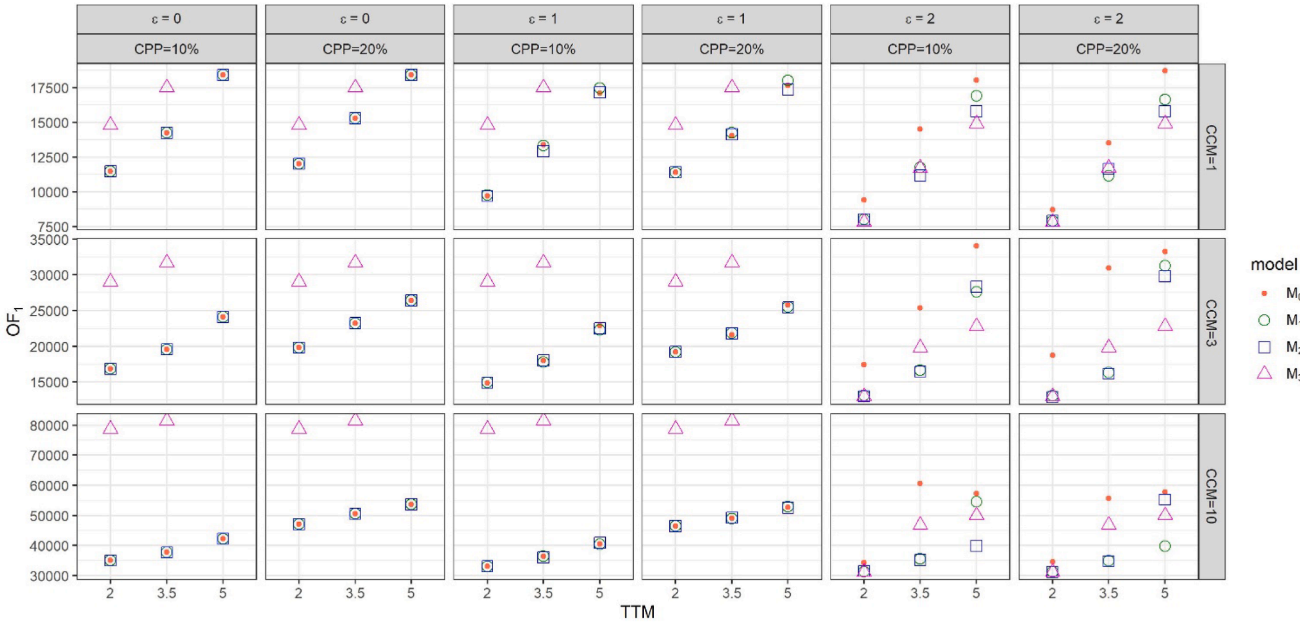

Fig. 2. Value of OF_1.

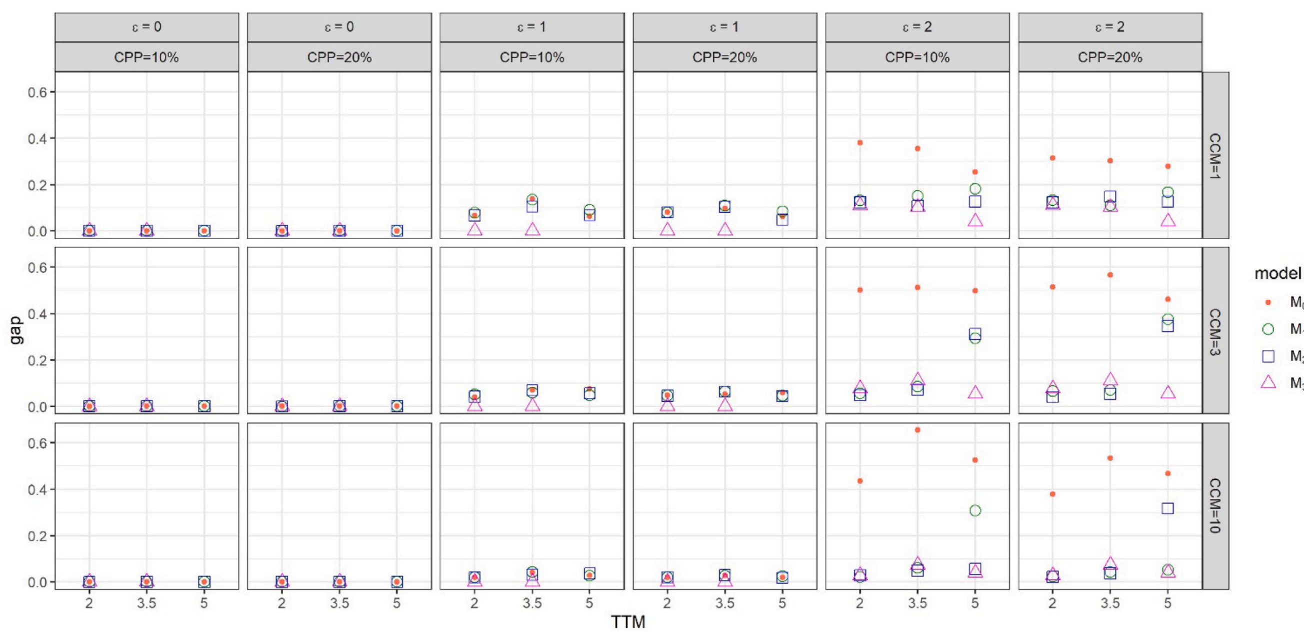

Fig. 3. Optimality gaps.

twice the sum of the daily operator cost (η) plus the daily center cost ($\eta \times$ CCM)). The values of these parameters were inspired by the real case.

With the stochastic model, we run 30 replications for each combination of the parameters in Table 9, each characterized by random adverse events. In this case, the gap limit was set to 5 % and the time limit to 2 h. We have chosen "extreme" CCM values to simulate scenarios in which the most impactful recourse actions (i.e., *resource activations*) have a very low (CCM=1) or very high (CCM=10) cost. CCM, in fact, is linked to both the cost of activating the center and the cost (χ) of activating an extra operator. Furthermore, due to the computational complexity of the stochastic problem, we reduced the scale of the problem by considering (see Table 7) a lower number of patients ($|P|=30$) and operators ($|O|=2$). Finally, we have tested the sensibility of our solutions to the parameter $|E|$ ($|E|$ in {3, 5, 7, 10}).

7. Results and discussion

7.1. *Deterministic models' comparison under different operating conditions*

Fig. 2 and Fig. 3 report, respectively, the value of OF_1 and the optimality gap (gap) for each combination of parameters ε, TTM, CCM, and CPP. Fig. 4, instead, reports the number of days when the center is booked, according to the models' solution. For benchmarking purposes, Fig. 4 also reports the results relevant to the auxiliary model (AUX). The number of days where the center is booked by AUX represents a lower

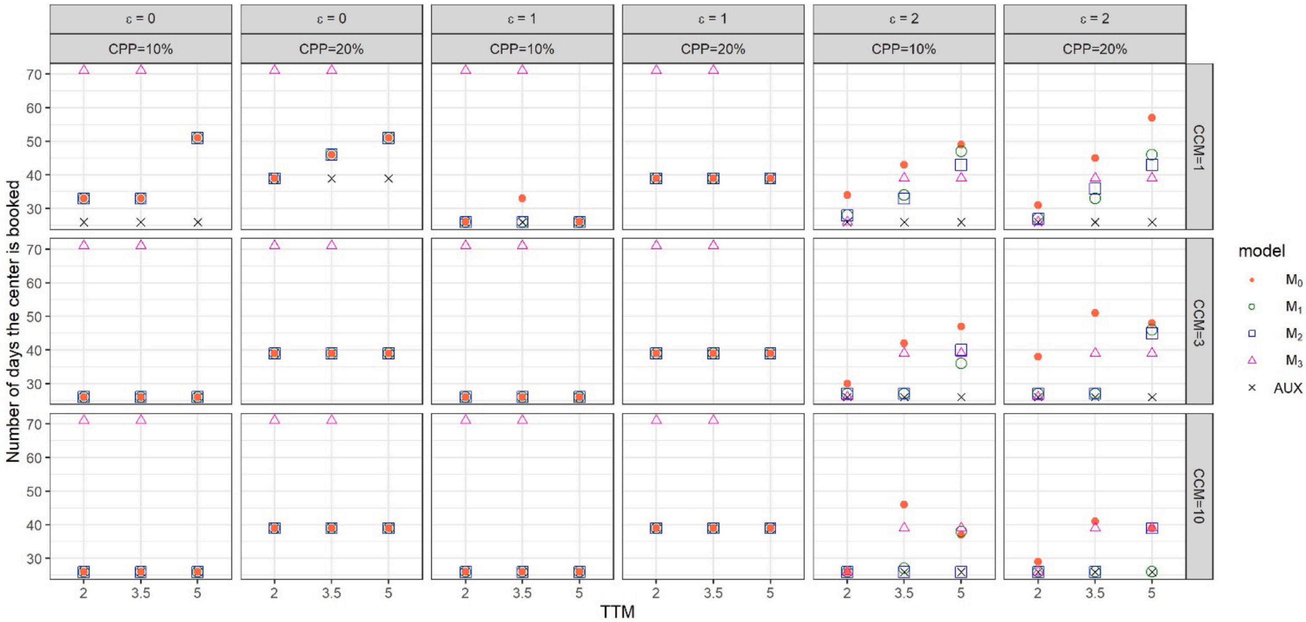

Fig. 4. Number of days the center is booked.

bound for the number of days the center is booked by the other models (see Section 4.3). It is worth pointing out that AUX model has always returned feasible solutions throughout the experimentation (i.e., not violating Constraint (30)).

7.1.1. Scenarios with ε=0

In these scenarios, the days when the treatments must be administered to each patient are known, and, consequently, the matheuristics do not allow for reducing the solution space. It is, therefore, not surprising that the M_0, M_1, and M_2 models return the same optimal solution and, consequently, the same value of OF (see the first two columns of Fig. 2 and Fig. 3). Such a value is significantly lower than the one, still optimal, returned by M_3. This means that, with $\varepsilon = 0$, letting the provider treat certain patients at home instead of treating all patients at the center (as M_3 would imply) allows for reducing costs. By making a row-wise comparison of columns 1 and 2 of Fig. 2, it can be noticed that the distance between the value of M_3's OF (triangles) and the ones of the other models (circles and squares) is larger when CPP is smaller (10 %). This is because when models M_0, M_1, and M_2 have fewer patients to mandatorily schedule at the center, they can better leverage the home care delivery to reduce to a minimum the number of days the center is open. This effect is magnified as the value of CCM increases. It is worth observing that when the treatment length is relatively high (TTM=5), M_3 returns no feasible solutions, while the other models do. This is because the capacity of the center is not enough to process all the patients needing care. With $\varepsilon = 0$, thus, resorting to home care allows for making up for insufficient center capacity at peak times.

Table 10
Percentage of treatments delivered after μ' days from the previous one.

ε	0	1			2				
μ'	14	13	14	15	12	13	14	15	16
M_0	100	8.2	81.8	10.0	27.2	3.9	38.7	2.9	27.3
M_1	100	9.3	81.0	9.7	21.0	1.5	65.6	1.6	10.3
M_2	100	9.5	80.4	10.1	21.0	1.6	67.0	1.3	9.2
M_3	100	0.0	100	0.0	27.9	0.0	40.3	0.0	31.9

7.1.2. Scenarios with ε>0

When ε increases, two contrasting effects emerge. On the one hand, the number of feasible solutions increases, and so does the possibility of finding solutions with a lower value of OF. On the other hand, the models' computational complexity increases (as the gaps in Fig. 3 show), thereby making it more complex for the solver to find good solutions within the set time limit (1 hour). It is worth noticing that the increase of the computational complexity is not linear moving from $\varepsilon = 0$ to $\varepsilon = 1$ and from $\varepsilon = 1$ to $\varepsilon = 2$. This is because of two effects: first, the number of model variables increases non-linearly with ε. Second, with $\varepsilon = 1$, shifting a treatment by one day leads to a violation of the patient's preferences (patients who prefer to be seen on even days may be seen on odd days and vice versa). Constraints (7) and (8) make it possible only a limited number of times ($\sigma_p$times for patients receiving treatments at the center and 0 times for those treated at home) in the planning horizon. With $\varepsilon = 2$, instead, treatments can be shifted two days forward or backward without violating any patient preference. Because of this, while with $\varepsilon = 1$, M_3 is not able to find a feasible solution for the scenarios in which TTM is high (as it happens for $\varepsilon = 0$), for $\varepsilon = 2$, M_3 finds feasible solutions for all scenarios. Table 10 shows, for each model and each value of ε, the percentage of treatments for which the time between two consecutive treatments is equal to μ'. The model widely employs the flexibility allowed by the tolerance. In fact, with $\varepsilon = 2$, the treatments are frequently scheduled with μ' = 12 or μ' = 16.

As can be noticed, with $\varepsilon = 1$, the percentage of treatments delivered exactly after μ=14 days from the previous one is larger than with $\varepsilon = 2$.

In general, holding all the other parameters fixed and increasing ε always allows for finding at least a solution that is characterized by an OF value smaller than the best solution obtained for a smaller value of ε, as can be observed by comparing columns 1, 3, 5 or columns 2, 4, 6 of Fig. 2. However, the model associated with such a best solution varies. With $\varepsilon \geq 1$, most of the models' solutions are nonoptimal and characterized by different bounds and optimality gaps (see Fig. 3). The causal mechanisms that make one model prevail over the others in different scenarios are described in the following section, distinguishing the scenarios with ε=1 from those with ε=2.

7.1.3. Scenarios with ε=1

When $\varepsilon = 1$ (columns 3, 4 of Fig. 2), the models M_0, M_1, and M_2

outperform M_3 even if M_3's solutions, when they exist, are optimal, while those of the other models are not (see Fig. 3). M_0, M_1, and M_2 are not significantly different from each other in terms of OF's values. In general, using models M_0-M_2 instead of M_3 always allows for eligible solutions and cost savings, and these savings are greater the more expensive the center. Models M_0, M_1, and M_2 return solutions in which the center is booked for the same number of days (which is way smaller than the one of M_3, see Fig. 4) and filled as much as possible with treatments on those days. The only exception is the scenario (CCM=1, TTM=3.5, CPP=10 %) where M_0 books the center for a number of days (33) that is greater than that returned by M_1 (26) and M_2 (26). However, since the cost of the center is relatively low, the overall cost of such a solution differs only marginally from the others.

7.1.4. Scenarios with ε=2

Results are less straightforward to interpret when ε=2 (columns 5 and 6 of Figs. 2, 3, and 4). The first thing to notice is that, across scenarios, M_0 returns solutions that are worse than those of the other models (Fig. 2). This is because the model, being less constrained, is more complex to solve, and the solutions found within the set time limit are characterized by gaps that are large in absolute value (from 0.25 up to 0.65) and way larger than those of the other models (Fig. 3).

For the scenarios in which ε=2 and TTM=2, the problem instances become rather simple, and M_3 outperforms all the other models. In these scenarios, since treatments are short, it is possible to schedule all the patients at the center just by using the residual capacity available on those days when the center must be, in any case, booked to treat center-only patients. In these cases, in fact, M_3 finds (optimal) solutions in which the center is booked for a number of days equal to the one returned by the auxiliary problem (26). The other models, instead, are not able to converge to such a solution within the set time limit. However, while M_1 and M_2 find solutions that are very close to those of M_3, M_0 does not. In this scenario, thus, activating the home care option does not allow for achieving any significant benefit.

For the scenarios in which ε=2, CCM≤3, and TTM=5, M_3 still outperforms the other models. This is because, other things being equal, when the treatment time is high compared to the travel time (TTM=5), it is more difficult to fit treatments into an operators' tour. Operators are likely to end their visits long before the end of the shift due to the inability to perform further treatment. In such a situation, if the daily cost of the center is low compared with the daily cost of the operators (CCM≤3), opening the center an additional day may be a better option than treating the patient at home. Interestingly, we observed that within the set time limit, M_3 finds solutions in which the center is booked for a number of days (39) that is equal to the lower bound that we obtained running the AUX model considering $P^c \equiv P$, (as we did with M_3). So, although the solver still does not certify it (gaps are slightly larger than 0), M_3's solutions are optimal, while the solutions of the other models are largely sub-optimal. This means that these scenarios are computationally demanding.

For the scenarios in which ε=2, TTM≥3.5, and CCM=10 (i.e., the non-trivial scenarios where the cost of the center is relatively high), M_1 or M_2 outperforms the other models. However, while M_1 and M_2 return similar results for TTM=3.5 (and those results are better than those returned by M_0 and M_3), their solutions differ a lot when TTM=5, based on the parameter CPP. Specifically, when CPP=10 %, M_2 outperforms M_1, while when CPP=20 %, M_1 is the best option. This is because, even if the treatment time is relatively large and CPP is low (10 %), booking the center based on the auxiliary model's solution and pre-assigning these patients to the booked days (as M_2 does), still leaves enough space to optimally frame other patients on those same days. This limits the need to open the center on other days, which is something most unwanted given the high cost of the center (in fact, for both M_2 and the auxiliary model AUX, the center is booked for 26 days). In addition, this reduces the computational complexity of the problem, which translates into a small optimality gap (gap(M_2)=0.06). On the contrary, booking the center based on the auxiliary models' solution without pre-assigning the patients necessarily needing the center (as M_1 does) leaves an exceedingly large number of feasible solutions to explore. In fact, within the set time limit, M_1 finds suboptimal solutions (gap(M_1)=0.31) with a high value of the OF (compared with M_2) due also to the fact that the center is booked for a much larger number of days (38). However, when treatments are long (TTM≥3.5) and there are many center-only patients (CPP=20 %), the suboptimal allocation of such patients obtained with M_2 makes it difficult to optimally frame other patients on those days and makes it necessary to book the center for a larger number of days (39). This also makes the model more complex to solve (gap(M_2)=0.32). In this scenario, pre-assigning only the days the center is booked based on the auxiliary model solution and letting the model choose when and where to schedule patients (as M_1 does) makes it possible to better saturate the center capacity in the pre-assigned days and avoid booking the center for additional days. In addition, it makes the model substantially easier to solve (gap(M_1)=0.04).

7.2. Comparison OF_1 vs. OF_2

In this section, we evaluate the effect of switching from OF_1 to OF_2 while at the same time introducing Constraint (*22*), i.e., we compare the results of the models M_0 and M_4. To do so, we consider the scenarios where ε=1 and we fix Δ=5 %. Thus, with M_4 we bind the total cost of the solution to be no more than 5 % larger than the corresponding M_0's one. Such an allowable cost increase ($\Delta\Omega$) can be seen as a "budget" model M_4 can rely on, to minimize patients' travel time while respecting all the other constraints. Table 11 reports the descriptive statistics of the percentage variation when switching from OF_1 to OF_2, of patients' and operators' travel time, and of the solutions' cost. Across scenarios, on average, such a switch allows for reducing the patients' travel time by 28.2 %. This translates into an average increase in the operators' travel time of 47.4 %. From Table 11, it is also possible to observe that the variation of the patients' travel time spans from −54.5 % to −5.2 % and those of the operators from 14.1 % to 115.64 %.

To understand the root causes of this variability, it is useful to look at Fig. 5.

The left panel shows the "budget" available to reduce patient travel time. The middle and right panels, instead, show, respectively, the percentage increase in the number of patients treated at home, and the percentage variation of the patients and operator travel time that occurs when switching from OF_1 to OF_2.

Due to space constraints, we show and comment only on the scenarios where CPP = 20 %, i.e., those characterized by the largest variability.

Switching from OF_1 to OF_2 causes two effects: (i) an increase in the net number of patients treated at home; (ii) a tendency to serve patients who live farther from the center at home. As CCM increases, the cost of the solution associated with OF_1 (Ω) increases, as well as the "budget" available to move patients from center to home care. Consequently, on

Table 11
Percentage variation when switching from OF_1 to OF_2.

Patients' travel time				Operators' travel time				Total costs			
Mean	Sd	min	max	Mean	Sd	min	max	Mean	Sd	min	max
−28.2	13.1	−54.5	−5.2	47.4	29.7	14.1	115.6	4.8	0.2	4.3	5.0

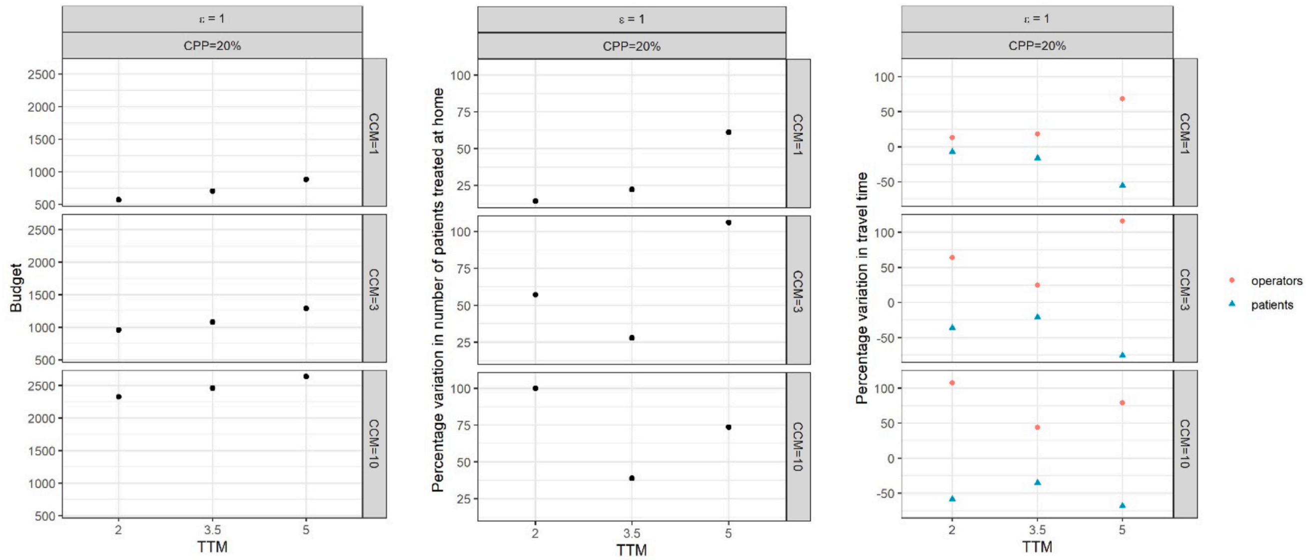

Fig. 5. Budget available to reduce the patient travel time (left panel). Percentage variation in the number of patients treated at home (middle panel) and in travel time (right panel) when switching from OF_1 to OF_2.

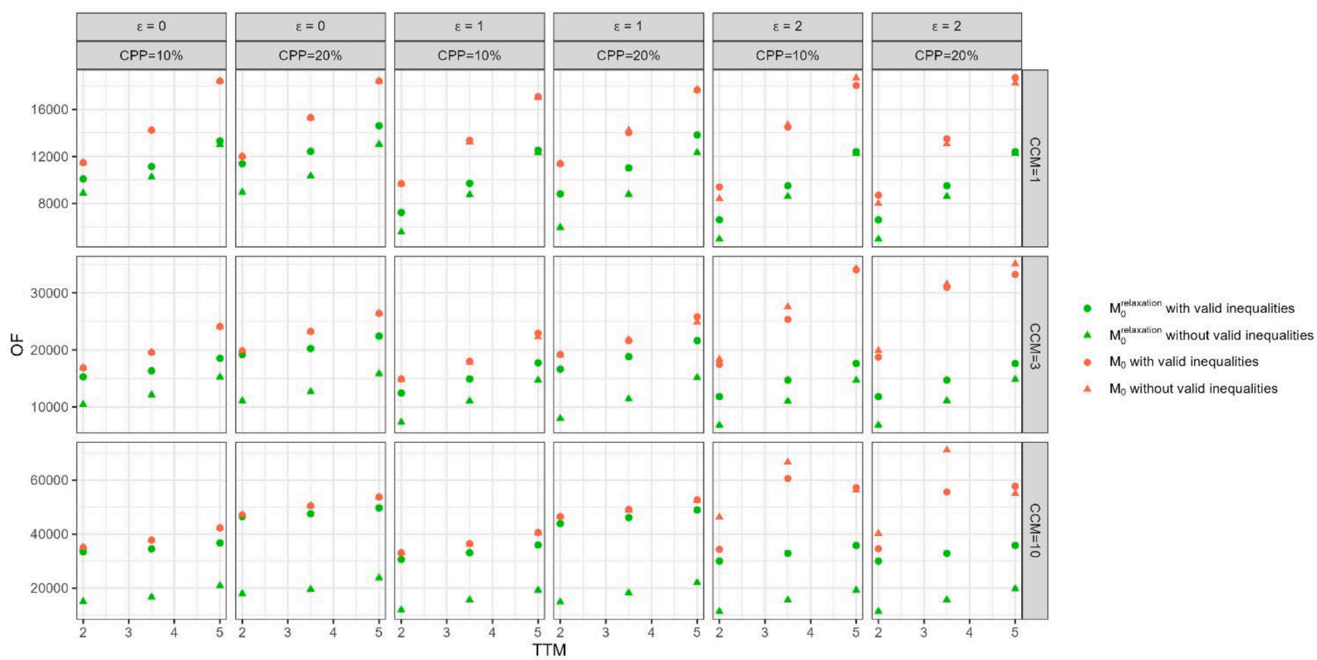

Fig. 6. OF at the root node and at the end of the time limit with and without the introduction of valid inequalities (27) and (28) into M_0.

average, the percentage of patients served at home increases, and the patient travel time decreases with CCM. The effect of TTM, instead, is ambiguous: on the one hand, increasing TTM increases the budget to serve patients at home, but on the other hand, it makes it less efficient to move a patient from center to home care. As TTM increases, the same reduction in patient travel time translates into a greater increase in provider travel time. In fact, if TTM is high, treatments last longer, and it is possible to serve fewer patients within an operator's tour. In our experimentation, the worst situation arises when TTM=3.5. Compared to the scenario TTM=2, the increase in the budget available to raise the operators' utilization is not enough to compensate for the decrease in the number of patients schedulable in a tour. Because of this, the dots in Fig. 5 (middle and right panels) for CCM≥3 show a non-monotonic trend.

7.3. Assessment of the effect of valid inequalities

To assess the effect of the valid inequalities (27) and (28), we compared the OF value of model M_0 and the OF value of M_0's continuous relaxation ($M_0^{relaxation}$) when the inequalities are included in the model and when they are not. The optimal solution of the relaxed problem provides a lower bound for the M_0's OF. An increase in the lower bound suggests a potential improvement in computational performance (although such improvement cannot be assumed with certainty).

The results are presented in Fig. 6 for all the scenarios commented on in Section 7.1. The experimentation was conducted under a time limit of 1 h.

As can be observed (compare green circles with green triangles), the introduction of valid inequalities considerably raises the value of the

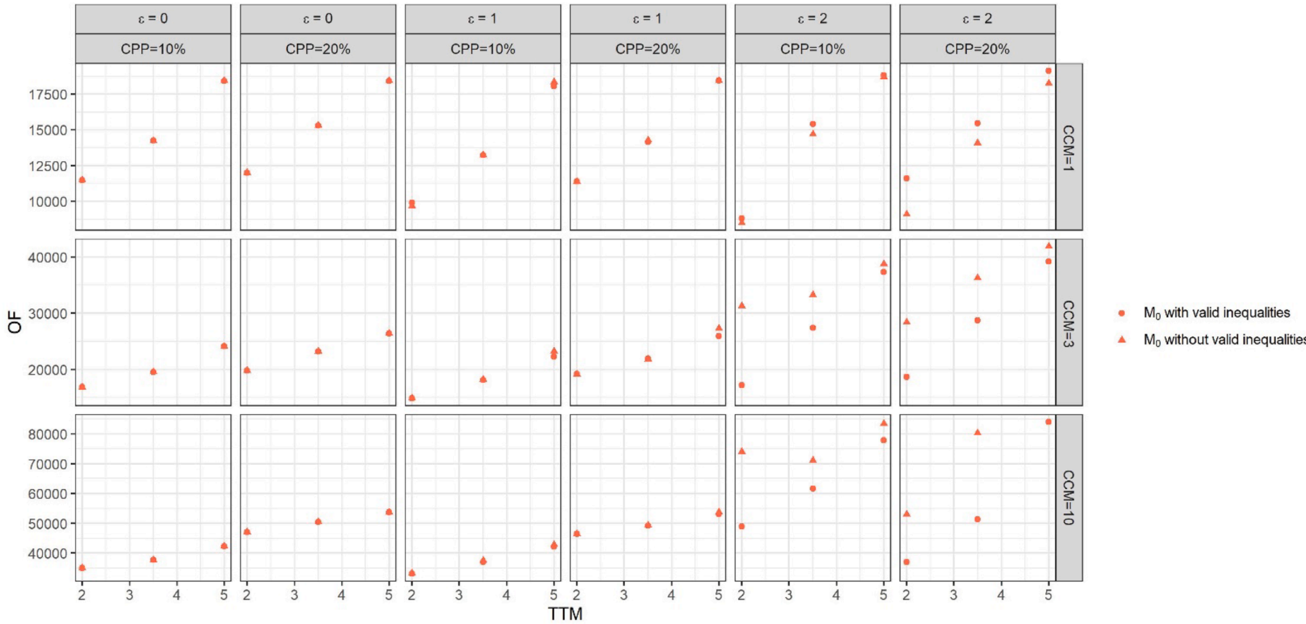

Fig. 7. OF after 10 min with and without the introduction of valid inequalities (27) and (28) into M_0.

Table 12
Error and overtime.

Model	Error (min) Mean	Sd	Range	Overtime (min) Mean	Sd	Range
M_0	−1.5	5.2	[−33.0,19.6]	0.0	0.1	[0,5.9]
M_1	−1.5	5.0	[−29.3,16.4]	0.0	0.1	[0,4.5]
M_2	−1.5	5.0	[−27.8,15.9]	0.0	0.0	[0,1.4]

lower bound (+64 % on average). Other parameters being equal, such an increase gets bigger as CCM gets higher (up to +197 % when ε=1, CPP=20 %, TTM=2, and CCM=10). On the contrary, valid inequalities do not significantly affect M_0's OF value after 60 min of computation (compare red circles with red triangles). However, by setting the time limit to 10 min, we can notice (Fig. 7) that the valid inequalities allow for a considerable decrease of M_0's OF value in the most computationally challenging scenarios.

We can conclude that the valid inequalities (27) and (28) improve the computational performance of the model and allow for obtaining better (yet suboptimal) solutions in a shorter amount of time for the most complex scenarios (i.e., with ε=2). In these scenarios, however, the optimality gaps are still very high (44 % on average, see Fig. 3), and it is preferable to use the matheuristics introduced in Section 4.3.

7.4. Assessment of the effects of approximating the travel time

Table 12 reports the mean, standard deviation, and range of variation (across operators and scenarios) of the *error,* defined as the difference between the approximated operator travel time calculated in the first phase and the actual travel time determined in the second phase (i.e. when the operator routing is determined via the TSP model). Results are not reported for M_3, which considers all treatments delivered at the center. Table 12 also reports the descriptives of the overtime that may arise if the actual travel time exceeds the approximated one.

As can be noticed, approximating the travel distances and times in the first phase leads to underestimating the operators' working time (the mean values of the error are negative) and to an error that is small and in favor of safety. As a result, overtime is rare and lasts only a few minutes. This approximation is, therefore, legitimate.

7.5. Assessment of the effects of embedding routing decisions in the baseline model

To assess the benefits that may arise from embedding routing decisions in the baseline model, we compared the results obtained from the model M_0^{routing} (which determines the operators routing) with those obtained using the M_0 to schedule patients and assign operators and subsequently determine the operator routing using a TSP (i.e., the two-phase approach described in Section 4). Such a comparison has been extended to all the scenarios presented in Section 7.1. As in the previous case, we set $T = 90$. However, to test M_0^{routing} also in less computationally demanding scenarios, we repeated the analysis with $T = 45$ days. Table 13 reports for each value of ε the mean total cost, the mean operator travel distance, and the percentage of instances solved within the set time limit with the two models. The mean values are calculated across all the scenarios sharing the same value of ε.

Table 13
Comparison between M_0^{routing} and M_0 in terms of mean total cost, mean travel distance, and % of solved instances.

T	ε	Mean total cost M_0^{routing}	M_0	Var %	Mean operator travel distance M_0^{routing}	M_0	Var %	% Solved M_0^{routing}	M_0
90	0	26,946.8	26,979.3	−0.1	744.6	798.8	−6.1	100	100
90	1	38,914.2	25,845.8	50.1	301.5	895.9	−54.0	83.3	100
90	2	29,207.7	32,237.9	3.7	0.0	540.0	−100.0	72.2	100
45	0	13,566.6	13,598.6	−0.24	360.9	414.3	−14.8	100	100
45	1	12,840.2	11,962.2	6.84	409.6	464.8	−13.5	100	100
45	2	12,173.3	8497.7	30.19	38.9	93.3	−140.1	100	100

As can be noticed, for $T = 90$, embedding routing constraints in the baseline model allows for a (very limited) decrease in the mean total cost (−0.1 %) only for the simplest scenario (ε=0). For this scenario, it also allows for a decent decrease in the operator travel distance. As scenarios get more computationally demanding (ε>0), however, M_0^{routing} is not able to return a good solution within the set time limit (1 hour), and quite frequently it is not able to find a solution at all. It is worth observing that when ε=2, M_0^{routing} returns trivial solutions where all patients are served at the center (operator travel distance=0).

With $T = 45$ days, instead, M_0^{routing} always finds an admissible solution even for ε>0. These solutions, however, are slightly better than those of M0 only for ε>0, as it happens with $T = 90$. The adoption of a two-phase approach is thus fully legitimate.

7.6. *Stochastic model*

This section presents the results of the experimentation inherent in the stochastic model. The section is structured in two parts.

In the first one, we use the *Value of the Stochastic Solution* (VSS) indicator (Birge and Louveaux [63]) to assess *ex-ante*, the expected benefit from solving a stochastic model rather than its deterministic counterpart [64]. This assessment helps understand whether utilizing a stochastic programming model is worthwhile, taking into account the associated efforts.

After determining the appropriateness of using a stochastic model, in the second part, we compare (as in M'Hallah and Visintin [65]) the benefits that would be possible to achieve, *ex-post*, if stochastic model solutions, rather than deterministic ones, were actually implemented.

7.6.1. *Ex-ante evaluation with CCM=10*

The VSS is defined as the difference between the optimal objective function value of the *Expected Value problem* (Birge and Louveaux [63]) and the optimal objective function value of the stochastic problem. We denote with M_E^{stoc} the stochastic model with |E| sets of adverse events defined in Section 5 and with OF(M_E^{stoc}) its optimal objective function value. The Expected Value problem is the stochastic problem M_E^{stoc} in which variables *x* and *f* are fixed according to the optimal solution of the deterministic model M_0. Indeed, by solving M_0, we obtain a first-stage solution, say $\widehat{x}, \widehat{f}$, that is also feasible for the stochastic problem M_E^{stoc} and we evaluate its cost. We denote with $M_E^{\text{stoc-fixed}}$ the Expected Value problem, and with OF($M_E^{\text{stoc-fixed}}$) its optimal objective function value. Thus, VSS = OF($M_E^{\text{stoc-fixed}}$) – OF(M_E^{stoc}) represents the goodness of the solution of the Expected Value problem when used as an approximation of the optimal solution of model M_E^{stoc}.

In Table 14, we report the results relevant to 30 random instances, where, for each instance, we solved the models M_E^{stoc} and $M_E^{\text{stoc-fixed}}$ for |E| in {3,5,7,10}. The table reports the mean and standard deviation of the objective function, the optimality gap, and resolution times. In addition, it provides the mean and standard deviation of the Center, Operators, and Travel costs. The first row reports the results relevant to the deterministic baseline model M_0.

The mean gap is satisfying for both the deterministic and the stochastic models, the resolution time is negligible for the Expected Value problems $M_E^{\text{stoc-fixed}}$, whereas the mean resolution time to reach the gap is quite high for M_E^{stoc} when $|E| \geq 5$. As expected, the resolution time for the stochastic model increases as |E| increases (even if from $E = 7$ to $E = 10$ such an increase is negligible), and so does the objective function. It can also be observed how the emergency cost associated with M_E^{stoc}, on average, is significantly smaller than that of $M_E^{\text{stoc-fixed}}$, while the center cost is slightly higher.

Table 15 reports the descriptive statistics of the VSS. As can be noticed, VSS is rather big (larger than 24 % of the mean value of the OF (M_E^{stoc}) across scenarios). This is an indication of the appropriateness of using a stochastic programming approach.

Finally, it is worth pointing out that because of the adverse events, across scenarios, on average, 6.3 % of the visits initially scheduled at home are rescheduled at the center (10.7 out of 170 on average).

Table 15
Descriptive statistics for VSS.

|E|	N	M(VSS)	Sd(VSS)	M(VSS)/ OF(M_E^{stoc})
3	30	11,722.0	3424.7	34 %
5	30	11,086.8	2309.2	31 %
7	30	9266.0	1932.5	24 %
10	30	9236.9	1573.0	24 %

7.6.2. *Ex-post evaluation with CCM=10*

Once the appropriateness of stochastic modeling had been checked, we carried out an extensive experimental campaign to assess the benefit stemming from its implementation.

The analysis was conducted as follows.

First, we considered scenarios where the cost of the recourse action *resource activation* is high (i.e., CCM=10). In these scenarios, the benefits of using a stochastic model should be magnified. For each of the above-mentioned 30 instances (indexed by *i*), we solved models M_E^{stoc} and we extracted the value of the variables *x* and *f*. Then we generated 30 sets (indexed by j) of random adverse events, and for each couple i, j we solved the Expected Value problem in which variables x and f are fixed according to the optimal solution of M_E^{stoc} run on instance i. The objective function value of the Expected Value problem represents the cost (hereafter *ex-post cost*) incurred by the provider to commit the resources

Table 16
Descriptive statistics for ex-post cost (CCM=10).

Model	N	M (ex-post cost)	Sd (ex-post cost)
M_0	900	46,219.2	3651.4
M_3^{stoc}	900	44,984.3	4038.7
M_5^{stoc}	900	43,903.8	3072.2
M_7^{stoc}	900	43,595.1	2615.8
M_{10}^{stoc}	900	43,122.1	2049.2

Table 14
Descriptive statistics for Objective Function, Optimality gap, and resolution time.

		Objective function		Gap		Time		Center Cost		Operators Cost		Travel Cost		Emergency Cost	
Model	N	M	Sd	M	Sd	M	Sd	M	Sd	M	Sd	M	Sd	M	Sd
M_0	1	29,575.6	–	0.0	–	40	–	20,000.0	–	8900.0	–	675.6	–	0.0	–
M_3^{stoc}	30	34,256.1	1402.3	0.0	0.0	151.3	209.8	22,400.0	1566.9	8967.8	242.2	631.7	15.3	1955.6	1238.1
M_5^{stoc}	30	35,999.0	1751.6	0.1	0.0	2585.8	3052.4	21,233.3	1546.6	8777.3	215.6	624.0	28.4	5045.3	1612.5
M_7^{stoc}	30	37,592.8	1627.8	0.1	0.0	6803.8	1514.4	20,900.0	2006.0	8788.1	191.0	625.3	31.7	6998.1	2021.6
M_{10}^{stoc}	30	38,088.8	1779.9	0.1	0.0	6855.2	1369.8	20,133.3	345.7	8895.0	127.1	632.6	9.5	8132.7	1689.8
$M_3^{\text{stoc-fixed}}$	30	45,978.1	3818.2	0.0	0.0	0.2	0.0	20,000.0	0.0	9046.7	230.4	652.4	27.6	16,255.6	3933.0
$M_5^{\text{stoc-fixed}}$	30	47,085.8	3276.4	0.0	0.0	0.2	0.0	20,000.0	0.0	9234.0	326.1	680.2	33.9	17,145.3	3424.8
$M_7^{\text{stoc-fixed}}$	30	46,858.9	2603.5	0.0	0.0	0.8	0.1	20,000.0	0.0	9200.0	302.0	673.0	32.3	16,961.0	2719.3
$M_{10}^{\text{stoc-fixed}}$	30	47,325.7	2227.8	0.0	0.0	0.9	0.1	20,000.0	0.0	9166.3	324.0	671.4	33.9	17,460.7	2325.0

Table 17
Lower and upper bound of 95 % confidence intervals for the difference between means (CCM=10).

Pairwise comparisons	*diff*	Lower bound	Upper bound
Mean ex-post cost (M_0) - Mean ex-post cost (M_3^{stoc})	1234,9	861.8	1574.0
Mean ex-post cost (M_0) - Mean ex-post cost (M_5^{stoc})	2315,4	2010.0	2630.6
Mean ex-post cost (M_0) - Mean ex-post cost (M_7^{stoc})	2624,1	2341.1	2911.5
Mean ex-post cost (M_0) - Mean ex-post cost (M_{10}^{stoc})	3097,1	2823.5	3375.2
Mean ex-post cost (M_3) - Mean ex-post cost (M_5^{stoc})	1080,5	753.7	1420.7
Mean ex-post cost (M_3) - Mean ex-post cost (M_7^{stoc})	1389,2	1062.2	1699.3
Mean ex-post cost (M_3) - Mean ex-post cost (M_{10}^{stoc})	1862,2	1561.6	2158.0
Mean ex-post cost (M_5) - Mean ex-post cost (M_7^{stoc})	308,7	52.7	586.3
Mean ex-post cost (M_5) - Mean ex-post cost (M_{10}^{stoc})	781,7	532.7	1028.4
Mean ex-post cost (M_7) - Mean ex-post cost (M_{10}^{stoc})	472,9	262.5	697.7

required by the *i th* M_E^{stoc}'s solution and to put in place the recourse actions needed to deal with the unexpected adverse events in the *j-th* set. Such a procedure allowed us to obtain, for each M_E^{stoc} a sample of 900 possible outcomes of their implementation, in terms of *ex-post cost.* Finally, to determine what would happen if we implemented the deterministic model, the same procedure was done starting from M_0' solution and generating 900 random sets of adverse events. Table 16 reports the descriptives of the ex-post cost associated with the implementation of each model across 900 scenarios.

To test whether these ex-post costs differ significantly, we first checked the parametric tests' assumptions. Levene's test led us to reject the assumption of homogeneity of variance (p-value <0.01) [66]. Therefore, we performed a bootstrap ANOVA with 5000 resamples [66]. The bootstrap ANOVA revealed a significant overall treatment effect (F-value= 0.000, p-value < 0.001), which implies a statistically significant effect of the model on the mean ex-post cost. Following the bootstrap ANOVA, we carried out bootstrap pairwise comparisons. Table 17 reports the bootstrap 95 % confidence intervals for the difference *diff* between means.

As we can notice, none of these confidence intervals crosses zero. We can thus conclude that, on average, as $|E|$ increases the ex-post cost significantly decreases. All the M_E^{stoc} models lead to lower ex-post cost than M_0. As for the effect size, we can observe that compared to M_0, M_3^{stoc}, M_5^{stoc}, M_7^{stoc}, and M_{10}^{stoc} allow, on average, a saving of 3 %, 5 %, 6 %, and 7 %, respectively. As a final remark, it is worth noting that as $|E|$ increases, the cost of the (ex-ante) solution increases, and the resolution time increases as well (Table 14). However, such a higher ex-ante cost and computational burden translates into a lower ex-post cost (Table 17), which is, indeed, the ultimate benefit sought by the provider.

7.6.3. Ex-ante and ex-post evaluation with CMM=1

To test whether it makes sense to use a stochastic model even in situations where recourse actions do not generate high costs, an analysis was conducted considering CCM=1. Hereafter we report the results for the most unfavourable situation for the stochastic model, i.e., the one in which $|E|=3$ (as we observed in Table 17). With the set parameters, M(VSS) and Sd(VSS) were equal to 2580.8 and 548.2, respectively. This implies that even when the cost of the *resource activation* is limited and $|E|$ is small, it still makes sense to use a stochastic model. The ex-post evaluation revealed that using the deterministic model leads, on average, to higher ex-post cost (M = 13,979.2, Sd=708.6) than the stochastic one (M = 13,540.7, Sd=604.4) and that the difference (*diff*) between these values is significantly larger than zero (we performed a bootstrap *t*-test with 5000 resamples, to test the null hypothesis H_o of *diff* =0, against the alternative hypothesis H_1 of *diff* ≥0 and we were unable to reject H_o, t = *3.826*, p = *0.001*).

8. Managerial insights

This study demonstrates that a provider, needing to cyclically administer specific treatment, over a medium to long planning horizon (e.g., three months), to a group of patients some of which cannot be seen at home, can achieve significant benefits by implementing an FC model. Enabling a provider to activate home care services can enhance patient satisfaction and minimize overall costs while also avoiding capacity issues.

In such a context, adopting a two-phase approach, where routing decisions are taken sequentially with respect to the assignment and scheduling ones, instead of a one-phase approach, where all these decisions are taken at once, can carry several advantages. In fact, while resulting in suboptimal solutions, a two-phase approach enables the independent handling of two distinct problems. Scheduling and assignment choices, which are crucial for organizing activities in advance, need early decisions, and models M_0, M_1, M_2, M_3, and M_4 are suitable to address these decisions in different operating conditions. In contrast, routing decisions can be deferred to accommodate the last-minute needs of patients or operators using a classic TSP model. In addition, a two-phase approach, being less computationally demanding, allows for finding better solutions within a reasonable time frame (1 hour) even if a tolerance is introduced in terms of time between two consecutive treatments (and only negligibly worse solutions when no tolerance is allowed, see comparison M_0 - $M_0^{routing}$ in Section 7.5). This is very important as, where this does not undermine the effectiveness of the treatment, introducing even a slight tolerance in the frequency with which treatments are administered (± 1 day) can significantly improve service quality in terms of care continuity and lead to significant cost savings (see Section 7.1, ε=1). Increasing the tolerance further (± 2 days), although it can still decrease the service cost, also considerably increases the computational complexity of the problem being addressed (see Section 7.1, ε=2). To capture the benefits associated with greater tolerance, it is advisable to use matheuristics M_1 and M_2 as an alternative to the optimal model M_0, as these provide better, albeit sub-optimal, solutions in a more affordable time frame. Specifically, M_1 is preferred to M_2 when the percentage of patients to be served at the center is high. In those cases, when both the cost to book the center for a day is similar to the daily cost of an operator (CCM≤3) and the treatment duration is large compared to the average travel time, it is advisable not to resort to FC model, but to use M_3 to schedule all patients at the center, as within a reasonable time frame such a model returns the best solutions. Our study also shows that accepting a modest increase in the total cost of service (∼5 %) can significantly reduce patients' total travel time (∼20 %) and, consequently, their satisfaction (see comparison M_4 vs M_0 in Section 7.2). Finally, our study demonstrates that if adverse events are a concern, it is advisable to use a stochastic model incorporating uncertainty concerning the occurrence of these events (M_E^{stoc}, see Section 7.6). When using stochastic models, considering a larger set of adverse events ($|E|$) leads to lower ex-post costs. However, this also makes the model more computationally demanding.

9. Conclusions

This study proposes novel deterministic optimization models to schedule cyclic treatments in FC settings using a two-phase approach where assignment and scheduling decisions are decoupled from the routing ones. In addition, it proposes matheuristics to gain efficiency when addressing complex instances. Furthermore, this study proposes a stochastic model to address uncertainties related to the occurrence of adverse events. The key findings of this study can be summarized as follows. (i) In most cases FC is to be preferred to CBC as it allows for making up for insufficient center capacity at peak times and better matching customer needs. CBC is preferable under two conditions: when the cost to book the center for a day is comparable to the daily cost of an operator and when the treatment duration significantly exceeds the average travel time. In these situations, the computational complexity of the problem does not allow any of the proposed models to find FC solutions outperforming CBC in a reasonable computational timeframe. (ii) The tolerance ε is a very important managerial lever. When possible, increasing ε allows significant savings but at the cost of a higher computational complexity. (iii) When computational complexity is an issue, it is preferable to use the presented matheuristics instead of the exact model. (iv) For the medium-term tactical problem considered, using a two-phase approach—where routing decisions follow assignment and scheduling decisions — rather than a one-phase approach — where all decisions are made simultaneously — is advantageous. In fact, within a reasonable computational timeframe, it allows for comparable or even better solutions. (v) If there are concerns about adverse events, employing a stochastic model rather than a deterministic one allows for finding more robust solutions and cost savings.

This work is not without limitations. First, we do not consider hybrid care solutions [67,68] in which, along the disease course, the same patient may be served both at home and at the center. Second, we consider service and travel times and the time between two consecutive treatments as known and deterministic (also in the stochastic model). Third, our experimentation refers to settings where travel distances and times are limited. Fourth, we assumed that all patients must be served and, consequently, we considered scenarios where there is enough capacity to serve them all. Fifth, we have not dealt with cases where servers provide different types of treatment at once [69,70]. Finally, we had to resort to downsized instances to deal with the computational complexity of the stochastic model.

Future research should thus address new service configurations (e.g., hybrid care, multi-treatment visits). In addition, they may also consider settings where patients are spread over a larger area and/or travel and service times are affected by significant variability and/or scenarios where capacity is limited, and additional decisions should be taken concerning the selection of the patients to serve. Finally, interesting avenues of research might be to employ exact techniques (like Branch-and-Price or Logic-based Benders decompositions) for solving the stochastic model on larger instances, and to employ a discrete event simulation to assess the robustness of the models' solution.

CRediT authorship contribution statement

Paola Cappanera: Writing – review & editing, Writing – original draft, Validation, Supervision, Software, Methodology, Formal analysis, Conceptualization. **Filippo Visintin:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Investigation, Formal analysis, Data curation, Conceptualization. **Sara Vannelli:** Writing – review & editing, Writing – original draft, Visualization, Validation, Software.

Declaration of competing interest

None.

Data availability

Data will be made available on request.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the author(s) used Grammarly to proofread the manuscript. After using this tool, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

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