

An appointment scheduling framework to balance the production of blood units from donation

Seda Başı^a, Giuliana Carello^b, Ettore Lanzarone^{c,*}, Semih Yalçındağ^a

^aYeditepe University, Industrial and Systems Engineering Department, Istanbul, Turkey

^bPolitecnico di Milano, Dipartimento di Elettronica, Informazione e Bioingegneria (DEIB), Milan, Italy

^cConsiglio Nazionale delle Ricerche (CNR), Istituto di Matematica Applicata e Tecnologie Informatiche (IMATI), Milan, Italy

Blood is fundamental in several care treatments and surgeries, and plays a crucial role in the health care system. It is a limited resource, as it can be produced only by donors and its shelf life is short; thus, the blood donation (BD) system aims at providing adequate supply of blood units to transfusion centers and hospitals. An effective collection of blood units from donors is fundamental for adequately feeding the entire BD system and optimizing blood usage. However, despite its relevance, donation scheduling is only marginally addressed in the literature. In this paper we consider the Blood Donation Appointment Scheduling (BDAS) problem, aiming at balancing the production of the different blood types among days in order to provide a quite constant feeding of blood units to the BD system. We propose a framework for the appointment reservation that accounts for both booked donors and donors arriving without a reservation. It consists of an offline Mixed Integer Linear Programming (MILP) model for preallocating time slots to blood types, and an online prioritization policy to assign a preallocated slot when the donor calls to make the reservation.

Keywords:

OR in health systems

Blood Donation Appointment

Scheduling Production balancing

Mixed Integer Linear

Programming model

Offline and online procedure

1. Introduction

Blood supply is a key point for all health care systems, as blood is necessary for several care treatments and surgical interventions. For example, in 2012, the annual need for blood was about 10 million units in the USA, 2.1 in Italy, and 2 in Turkey. Blood is also a limited resource because, at present, it cannot be produced in laboratory but only by humans. Thus, in Western countries, blood is usually collected from donors, i.e., unpaid individuals who donate their blood voluntarily. Further, its short shelf life limits the period between donation and utilization, thus preventing long term storage.

Blood is provided through the Blood Donation (BD) system, which is in charge of providing an adequate supply of blood units to transfusion centers and hospitals. Due to the short shelf life, BD system should meet the overall blood demand from hospitals and transfusion centers, but at the same time it should follow the temporal profile of the demand to avoid blood shortage and wasted units. The BD supply chain can be divided in four steps, as shown in Fig. 1: *collection, transportation, storage and utilization* (Sundaram

& Santhanam, 2011). Blood is first collected: donors are registered and visited by a physician to assess their eligibility for donation and, if eligible, they make the donation. Once the blood is gathered, tests are performed on each blood unit to prevent infectious diseases. Afterwards, blood units are transported and stored. Blood components are then distributed to hospitals and transfusion centers based on their inventory levels. Finally, blood is transferred to the end users (the patients) for transfusion.

In this paper, we focus on the blood collection step, which represents the first (and most critical) step of the BD supply chain. Not only increasing the number of donations improves the throughput of the BD system, but also an effective management of donors' arrivals among the days may improve the performance of the system and provide a reliable supply of blood units in agreement with the storage requests. In fact, the role of a blood collection center is to provide a reliable supplying of blood units to the storage, in agreement with the storage request.

There are two main storage policies, i.e., to store enough blood units to cope with any blood demand at any time, or to satisfy the demand from a hospital or a medical center while keeping the stored amount of blood units limited. Balancing the production, i.e., producing a constant number of blood units over the days, is the main goal in several cases when the customer is a large hospital with several elective patients, a low variable demand for

* Corresponding author.

E-mail address: ettore.lanzarone@cnr.it (E. Lanzarone).

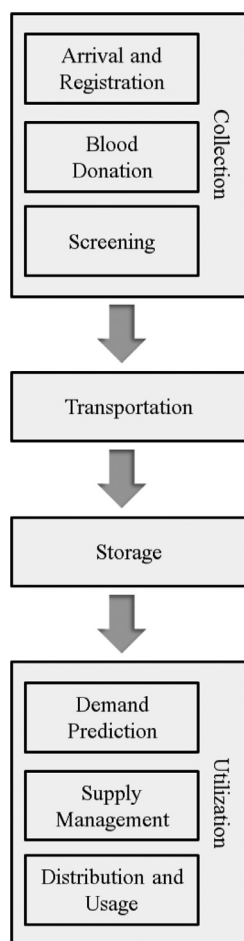


Fig. 1. Steps of the BD supply chain.

blood, and well-dimensioned storage capacity. Alternatively, production profiles can be defined in accordance with the (free and committed) storage capacity. See Puranam, Novak, Lucas, and Fung (2017) for an analysis of blood inventory, where they derive optimal ordering policies for an inventory system under multiple independent sources of supply.

Several blood collection centers are starting to implement a reservation system. In fact, reserving the donation appointment can reduce donors' waiting time and, thus, guarantee a better service to donors, which may help in increasing the number of donors and the frequency of donation. Moreover, by appropriately addressing donors to a suitable day, reservation may also balance the production of blood units among the days. In any case, centers also accept donors without reservation not to refuse any possible donation, because of the high need for blood units and to prevent donors from feeling that their donation is not important. Thus, generally speaking, both booked and non-booked donors are usually present in the collection centers, even though the effort is to increase the rate of booked ones. So far, appointments are manually assigned in the majority of collection centers where reservation is possible. Manual management may be able to reduce donors' waiting times and to take their preferences into account; however, it is short-sighted and may prevent from effectively balancing blood unit production.

In this work, we propose an appointment scheduling system for blood donation to balance the production of blood units of the different types (combination of group and Rhesus factor) among days, while taking into account both booked and non-booked donors. The proposed architecture for planning the assignments consists

of two phases, i.e., an offline preallocation of time slots for donation and an online allocation of them, where a *time slot* is as an operational or service time interval suitable for a donor. The preallocation phase is responsible of reserving slots to the blood types, while the allocation phase is responsible of assigning a suitable preallocated slot to each donor when he/she calls for reservation. In other words, the preallocation phase prepares a number of spare slots for the different blood types, which are then used for the successive online booking phase. The architecture is based on a Mixed Integer Linear Programming (MILP) model for the preallocation phase and a prioritization policy for the allocation phase.

Although the problem shares some features with other health care related appointment scheduling problems, balancing the production is not a common objective. Moreover, the characteristics of the BD system make the donation scheduling different from other appointment scheduling systems in different fields. Thus, to the best of our knowledge, this paper is the first attempt to deal with what we can define as the Blood Donation Appointment Scheduling (BDAS) problem.

In this paper, we particularly consider the case of the Milan Department of the *Associazione Volontari Italiani Sangue* (AVIS), denoted as AVIS Milan in the following, which serves a large hospital with a quite constant demand for blood. AVIS is the largest network of BD collection centers in Italy, and AVIS Milan is one of the largest centers in the network. Moreover, it can be considered as a general center, since it shares many features in terms of donors, activities and management with several other centers. Thus, the approach proposed in this paper can be considered as general and applicable to other blood collection centers (Baş, Carello, Lanzarone, Ocak, & Yalçındağ, 2016).

The paper is structured as follows. The BDAS problem is described in Section 2. Then, a literature review on BD collection management and appointment scheduling is presented in Section 3. The proposed architecture for the BDAS problem is detailed in Section 4, including the MILP preallocation model and the prioritization policy. An analysis of the MILP preallocation model is further reported in Section 5. Finally, the computational tests performed on the AVIS Milan case and the conclusions are reported in Sections 6 and 7, respectively.

2. Problem description

The BD collection phase includes all of the stages between donor's arrival and the complete preparation of the blood unit. The process starts when the donor arrives at the blood collection center. Here, donors are visited by a physician to assess their eligibility for donation; if eligible, donors make the donation. Once the blood is drawn from an individual, it undergoes a screening process to be searched for any infectious diseases, and the blood units that pass the tests are sent for storage.

Two main aspects are present in the blood collection step. On the one hand, managing a BD collection center includes the typical operational problems that are common to several service providers and other health care facilities (e.g., visit centers, hospitals, emergency services). Among them, we mention workforce planning, appointment scheduling, demand prediction, waiting times reduction, service quality improvement, etc. On the other hand, the goal of a BD collection center is to produce blood units and blood products to meet the demand from the health care system. Thus, an effective management of a collection center must account for the production of blood units in addition to its internal organization as a service provider. An effective management of blood collection is firstly necessary to increase the throughput and keep the costs sustainable. However, a more general view should include an effective management of donors' arrivals throughout the days to optimize the daily production of blood units with respect to the storage

requests. Neglecting this point may result in an unbalanced feeding of blood units to the rest of the BD supply chain, with consequent blood shortage and wasted units. The first point (throughput and costs) is sometimes addressed in the literature; on the contrary, more structured strategies that also include the impact on the whole BD chain are still lacking (see Section 3).

In practice, appointment scheduling decisions are manually made or supported by short-sighted tools. Even though these tools are able to reduce donor waiting times and physician overtimes, and/or optimize other operational issues, they do not include any analysis of the daily blood production with respect to the storage while allocating time slots to donors. Hence, the main goal and benefit of a comprehensive scheduling system is to combine these contrasting needs: to improve the operational level while providing a reliable supply of blood units in agreement with the storage requests. This is actually the goal of this paper.

From a management point of view, donors can be mainly divided in two groups: *returning donors* who donate on a regular basis, and *walk-in donors* who occasionally donate or donate for the first time. In any case, a donation can be made after a rest period from the previous one, which is defined by law. If the blood collection center has a reservation system, donors can be further classified as *booked* and *non-booked* donors.

As mentioned, we consider the case of AVIS Milan. AVIS was founded in 1927 and nowadays is the largest blood donors' association in Italy, bringing together over one million of voluntary blood donors across the country. AVIS Milan covers the territory of Milan and is in charge of collecting blood for one of the main hospitals in Milan, i.e., the Niguarda hospital; in the last 4 years, it provided

on average about 50 whole blood donations per day, with a total of about 18,000 donations per year.

AVIS Milan is starting to implement a reservation system and currently accepts donors with and without reservation. The latter are the majority at the moment, but AVIS Milan aims at increasing the rate of the booked donors. Its goal is to produce a constant amount of blood units for each blood type along with the days. In fact, Niguarda is a large hospital with a lot of elective surgeries and a quite constant amount of emergency requests. Thus, the request from Niguarda hospital is to feed the system with a constant (and possibly high) daily amount of units of the different blood types, even if unpredictable demand peaks may occur in specific periods and conditions. On the contrary, the lack of a constant feeding is the actual bottleneck of the entire system in practice, as explained by the AVIS Milan staff.

The current architecture of the AVIS Milan scheduling system is shown in Fig. 2 (a), which also shares many features with several blood collection centers. Some donors call to book the donation day and time slot beforehand, and slots are assigned (booked) until a maximum percentage of the daily capacity is reached, regardless of blood type. The daily capacity is expressed in terms of the total physician working time without incurring overtime. In fact, while AVIS Milan has a large donation room where a seat is quite always available when a donor arrives, the physician's visit before donation is the bottleneck of the system that generates the queue; thus, we consider the physician working time as the scarce resource and the time slot refers to the time spent for the visit. Some part of the capacity (a maximum percentage) is usually taken into account when a donation is booked, to preserve space

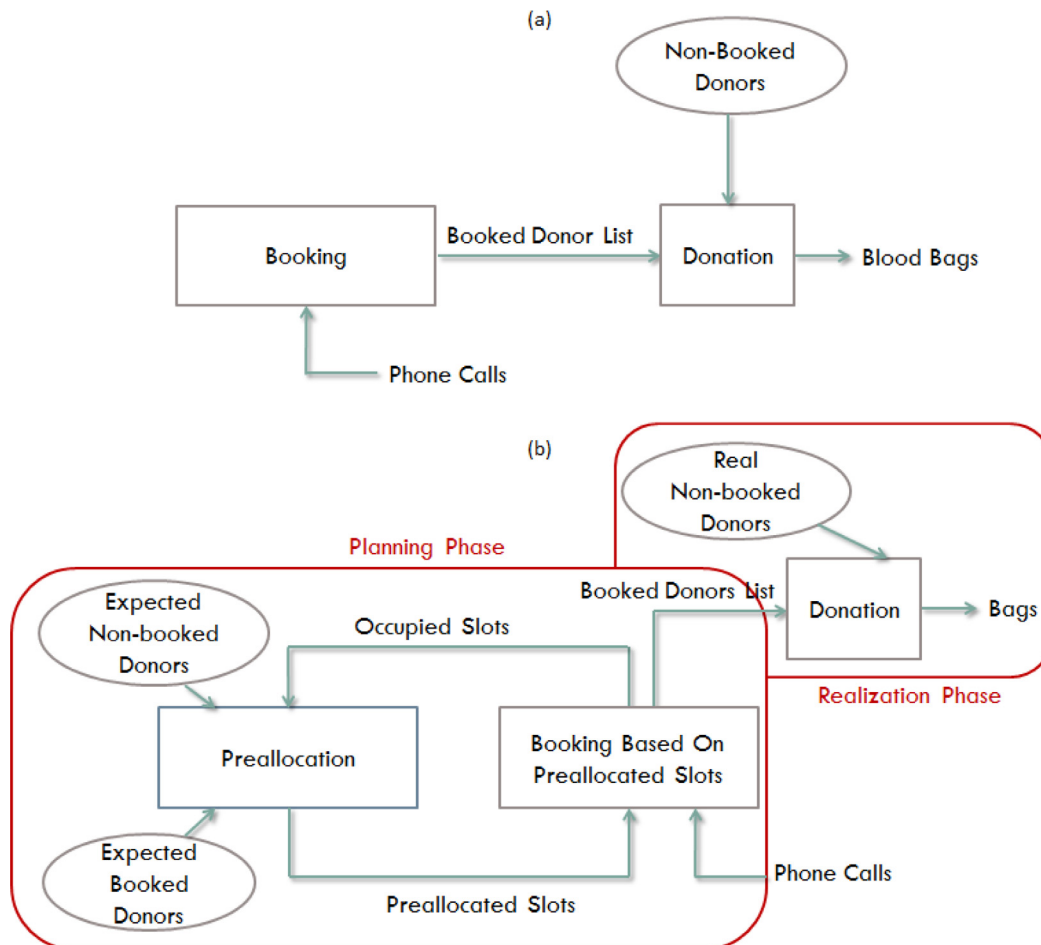


Fig. 2. Current architecture of AVIS Milan (a) and proposed architecture (b).

for non-booked donors; however, to match the donors' preferences, this threshold can be extended (overpassed) without penalties. The daily donations are finally given by the amount of booked and non-booked donors who show up at the blood collection center.

Historical data from AVIS Milan show that the number of produced units is not constant among days. Fig. 3(a) reports the daily number of whole blood units produced per day, and Fig. 3(b) the relative percentage of units with type A Rh+ (data refer to 2013 and 2014, i.e., two years in which production balancing was not considered). We can observe that the number of blood units is not evenly balanced among the days, despite the goal of flattening the production both in terms of total number of units per day and for the different blood types. In particular, AVIS Milan would like avoiding high frequency oscillations, while low frequency oscillations do not depend on scheduling and cannot be avoided. For example, the decreased production around days 220–240 in Fig. 3(a) corresponds the month of August when people are usually on holiday and they do not donate.

3. Literature review

In literature, there are two main classifications of the BD supply chain and the related management problems. Sundaram and Santhanam (2011) classify the system based on the main steps of a blood unit life (as mentioned in Section 1) while, according to Pierskalla (2005), the BD supply chain can be classified based on the strategic and tactical operational decisions. Many optimization problems are present in managing the BD supply chain, from donation to final utilization of blood units. Most of them have been largely addressed in the literature, as underlined by recent surveys; e.g., Beliën and Forcé (2012) reviewed the literature up to 2010, and Osorio, Brailsford and Smith, (2015) presented a structured review on quantitative modeling for BD supply chain. However, the different problems related to the BD supply chain management have received different attention in the literature. In particular, even though blood collection step is one of the most important steps in the chain at the operational level, the BDAS problem has never been addressed so far. In fact, a literature analysis on BD supply chain management conducted by Baş et al. (2016) and then updated up to August 2015, which included 177 papers that are available on Scopus and the other main scientific databases, shows that only the 1% of the BD management investigations deal with donor arrival and scheduling.

In the following, we first review the literature dealing with the management of the blood collection step, and then we survey the literature about appointment scheduling systems.

3.1. Blood collection in the literature

Several management problems arise in the blood collection, which can be classified based on the planning (e.g., location of blood collection centers and staff dimensioning) or operational (e.g., appointment scheduling, screening policies, donation prediction) level. Although problems of both levels have an impact on the entire BD chain, problems occurring at the operational level have a direct effect on blood shortages and wasted units. In the following, we focus on such level, which is closely related to the appointment scheduling system developed in this paper.

Michaels, Brennan, Golden, and Fu (1993) developed a simulation study to evaluate scheduling strategies for donors who arrive at a Red Cross blood drive, and compared them in terms of mean transit time to find out the most effective one. Testik, Ozkaya, Aksu, and Ozcebe (2012) identified donor arrival patterns and employed a queuing network model of the donation process to dimension the workforce. Alfonso, Xie, Augusto, and Garraud (2012); (2013) proposed Petri net models to describe all rel-

evant donor flows in various blood collection systems. Do Carmo, Gurgel, Carmo, Freires Saraiva, and de Sena (2013) proposed a demand forecast model and a management model for sizing the inventory of blood products in a blood bank in Brazil. Mobasher, Ekici, and Özener (2015) coordinated appointment and pick-up times at blood donation sites to maximize platelet production. Elalouf, Hovav, Tsadikovich, and Yedidsion (2015) improved the structure of a three-echelon blood sample collection chain, which includes clinics, centrifuge centers, and a centralized testing laboratory. Şahinyazan, Kara, and Taner (2015) developed a vehicle routing for a mobile blood donation system, with the primary objective of increasing blood collection levels. Osorio, Brailsford, Smith, Forero-Matiz, and Camacho-Rodríguez (2016) presented an integrated simulation–optimization model to support strategic and operational decisions in blood production planning.

More closely to the BDAS problem, Alfonso, Xie, and Augusto (2015b) presented a simulation–optimization approach for capacity planning and appointment scheduling in blood collection systems, accounting for random service times, random arrivals of walk-in donors, and random no-shows of scheduled donors. The aim is to maximize donor service level and minimize system overtime simultaneously. However, different from the proposed BDAS problem, they did not take into account the production balancing of each blood type, which is instead our main goal. Moreover, Alfonso, Augusto, and Xie (2015a) proposed a two-step collection planning framework for mobile collection centers. The first step is the annual planning of the collection period for each mobile site, while the second deals with the detailed weekly plans, i.e., the collection days at each mobile site and the corresponding transfusion teams. On the contrary, in the considered BDAS problem, we address the assignment of slots to donors for a prereservation of the appointments under fixed (non-mobile) collection centers and given work-force size.

Prediction models for the waiting time and other random variables related to blood collection are also available. Flegel, Besenfelder, and Wagner (2000) developed a logistic regression model to compute the donation probability within a given time frame. Ferguson and Bibby (2002) used a prospective design to predict the number of future blood donations. Borkent-Raven, Janssen, and Van Der Poel (2010) estimated the blood supply from donations using annual donor retention rates and mean numbers of donations per donor and year. Boonyanusith and Jittamai (2012) investigated donor behavior patterns and the factors that influence donation decision. Ritika (2014) found a fair classification technique for donation prediction. Van Dongen, Ruiters, Abraham, and Veldhuizen (2014) analyzed the factors that affect the intention to continue donating in new donors. Van Brummelen, De Kort, and Van Dijk (2015) developed a model for estimating the waiting time in blood collection sites, which provides the total delay time distribution. Fortsch and Khapalova (2016) proposed a Box–Jenkins method to predict blood demand, aiming at lowering costs and reducing blood wastages.

3.2. Related appointment scheduling systems

Scheduling problems are widely studied in the literature (Gupta & Starr, 2014) and have been classified according to several criteria (e.g., number and sequence of machines, processing times, job arrival rates and objective function) for both manufacturing and service systems, including health care systems.

Effective schedules are widely studied in manufacturing (Han, Zhang, Lu, & Lin, 2015; Jonsson & Ivert, 2015; Oyetunji, 2009; Pinedo, 2009; 2012; Rahman, Sarker, & Essam, 2015; Sawik, 2011) with the goals of meeting due dates, maximizing machine or labor utilization, and minimizing job lateness, response time, completion time, time in the system, overtime, idle time and work-

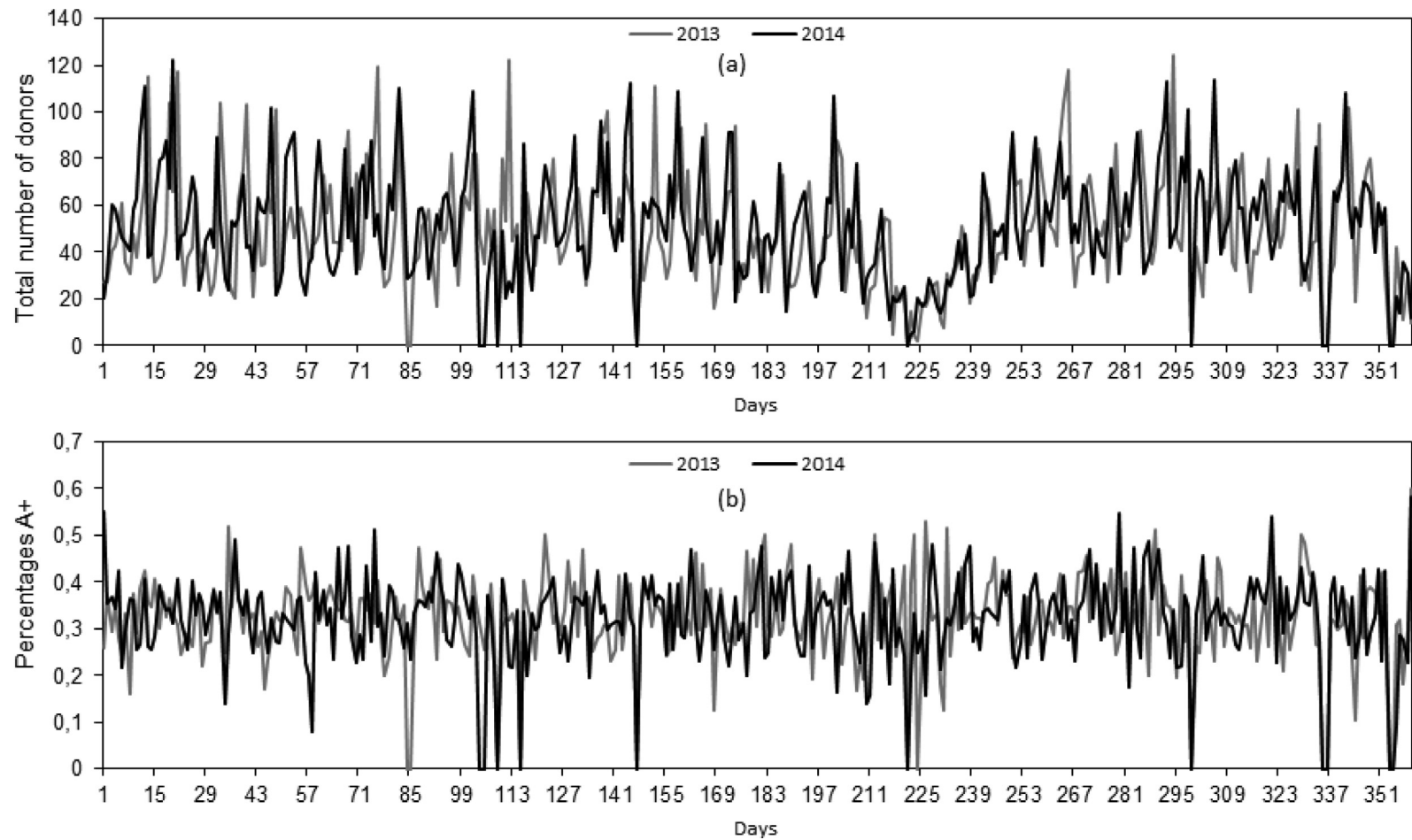


Fig. 3. Daily number of whole blood donations in 2013 and 2014 according to the historical information of AVIS Milan: total number of donations (a) and percentage of type A Rh+ (b).

in-process inventory. A review can be found in Framinan and Ruiz (2010).

Scheduling in service systems is different from that in manufacturing, mainly because the system capacity in manufacturing may exploit inventories. On the contrary, a service is provided together with its utilization; consequently, service capacity cannot be stored and it is lost if unused (Ayvaz & Huh, 2010; Zhou & Zhao, 2010). In service systems, customers want to spend the minimum waiting time and receive good quality service, whereas service providers want to perform the schedule with minimum cost. In particular, service systems try to satisfy the demand through appointments. Thus, appointment scheduling represents the interface between demand and service provider.

Focusing on health care services, many papers dealing with appointment scheduling are available in the literature (Liu, 2009; Truong, 2015; Wang & Fung, 2015). The goal is usually to maximize the number of patients while minimizing waiting times, physician idle times and overtimes (Gupta & Denton, 2008; Samorani & LaGanga, 2015). Some papers analyze the negative effects of no-shows in terms of provider underutilization and delayed patient access (Liu, 2016; Liu & Ziya, 2014; Robinson & Chen, 2010); in such cases, most of the applied solutions propose overbooking in order to increase the utilization.

The management of the operating theatres has been one of the most studied topics in the last 60 years (Cardoen, 2010; Hans & Vanberkel, 2012). Other widely studied topics are nurse scheduling (Bai, Burke, Kendall, Li, & McCollum, 2010; Burke, De Causmaecker, Berghe, & Van Landeghem, 2004; Lim, Mobasher, Kardar, & Cote, 2012), patient appointments in ambulatory care (Gupta & Wang, 2012), appointment scheduling in outpatient clinics (Berg & Denton, 2012), bed assignments in hospitals (Hall, 2012), scheduling of urgent patients (Gerchak, Gupta, & Henig, 1996; Klassen & Rohleder, 2003; Torkki, Alho, Peltokorpi, Torkki, & Kallio, 2006), nurse and surgery scheduling (Beliën & Demeulemeester, 2008), and trade-offs between the cancellation of scheduled elective surgeries to accommodate urgent arrivals (Zonderland, Boucherie, Litvak, & Vleggeert-Lankamp, 2010).

Blood collection involves both the features of a service system and those of a production system. Thus, the BDAS problem cannot be included by the ordinary classification, and this also explains the lack of BD appointment scheduling systems in the literature.

4. Proposed architecture for the donor appointment scheduling

In this paper, we propose a new architecture for the BDAS problem. As mentioned in the Introduction, the proposed architecture for planning the donations consists of two phases, i.e., an offline preallocation of time slots for donation based on the blood type, and an online allocation. The output of the preallocation acts as an input for the allocation, in which the daily layout of prereserved slots is filled while the donors call for booking. Indeed, the allocation phase assigns a preallocated slot to each donor, when he/she calls for reservation, among those prepared in the preallocation phase. Such decomposition in two phases is based on the evidence that, in order to balance the daily production of all blood types, the slots should be assigned in advance to the different types and then the donors should be addressed to the slots of their specific type.

The list of preallocated slots is refreshed (regenerated) after a certain number of reservations are received and/or at a fixed frequency (e.g., each day). The number of preallocated slots which have been converted in reserved slots is fed back to the preallocation phase (the assigned slots are no longer available and have to be considered as occupied) and the process is repeated. As a result, the plan for each day is given by the list of booked donors

for that day, together with the number of empty slots that are left free for the non-booked donors who may arise to donate.

Besides the goal of production balancing, the daily layout of prereserved slots should meet some other requirements: the total number of slots should be around the expected number of donors, the slots should respect the proportions of the blood types, and an appropriate number of spare slots should be preserved for non-booked donors. To meet these requirements, the future amount of donors (both booked and non-booked) is required and should be predicted, e.g., based on the available historical data.

The proposed architecture is summarized in Fig. 2(b). The preallocation phase receives the expected number of booked and non-booked donors, together with the number of occupied (already booked) slots, and provides the preallocated slots x_t^b (i.e., number of preallocated slots for blood type b at day t of the time horizon). Then, the allocation phase uses these preallocated slots to respond to the phone calls for reservation, and updates the list of occupied slots.

As mentioned before, the preallocation phase is based on an MILP model whereas the allocation phase assigns a prereserved slot to each donor with a prioritization policy. They are detailed in the next two sections.

4.1. Optimization model for the preallocation of slots

The preallocation of the slots is optimized through an MILP model, whose aim is to preallocate a balanced number of slots for each blood type close to the expected number of booked donors in the considered time horizon. While doing so, some spare time slots are left for non-booked donors, physicians' peak loads are dispersed within each day by means of periodic physician capacities, and the total system capacity is restricted by considering maximum daily physician capacities.

A set of days T represents the considered time horizon, and all days $t \in T$ are divided in a set K of periods. Moreover, the set of blood types is denoted as B . We consider for each day t and each blood type b a number of slots x_t^b to preallocate (non-negative integer decision variable) and a number of already allocated slots a_t^b coming from previous reservations (integer parameter).

We assume an expected number d_b of booked donors for blood type b over T . Ideally, for each blood type, the summation over T of the already booked slots and the slots to preallocate should be equal to d_b , i.e., $\sum_{t \in T} (x_t^b + a_t^b) = d_b$. However, as mentioned, we do not know the exact number of booked donors in advance. Thus, we include a flexibility degree in complying with the summation by imposing that $\sum_{t \in T} (x_t^b + a_t^b)$ can lay in the interval from $(1 - \varepsilon)d_b$ to $(1 + \varepsilon)d_b$ for each blood type b . Parameter ε ($0 \leq \varepsilon \leq 1$) is an index of the associated flexibility: small ε values close to 0 refer to low flexibility, whereas higher values can be assumed in case of highly unknown donor arrivals. Forcing the system to allocate a given number of slots (actually a number in a range) is necessary in the presence of an objective function that aims at balancing the production of blood units among days and at avoiding periodic accumulation of donors. In fact, on the one hand, a perfect balancing with no overtime can be obtained with a null production. On the other hand, preallocating a number of slots higher than the necessary amount will lead to several empty slots because of fewer calls for reservation; thus, even though the preallocated slots are balanced, the actually occupied slots could be unbalanced. Hence, an appropriate selection of ε value is crucial, and too high values are not of interest for a practical application, meaning no information about the d_b parameters. In particular, we remark that high values of ε close to 1 may nullify the number of preallocated slots or generate an unnecessary higher number of slots.

As indicated above, an amount of slots should be left empty for non-booked donors, which is represented by n_t^b for blood type b

and day t . Since non-booked donors may arrive in any period k of the day ($k \in K$), the fraction of non-booked donors for period k is denoted with α_k (we assume the same division $\forall t \in T$).

The standard time r required for the visit of a donor (considered while allocating new slots x_t^b) is assumed to be constant and equal for all donors. In addition, for the already booked slots a_t^b , a specific service duration can be set for each donor; we denote by R_{tk} the total time for the already allocated donors in period k of day t . Note that, at each day t , the number of already allocated slots a_t^b are grouped by blood type b , while the associated times R_{tk} are grouped by period k .

The overall capacity of the physicians in period k of day t is denoted by c_{tk} , and the service time required at day t and period k above the capacity c_{tk} is denoted by p_{tk} . We refer to p_{tk} as a *dispersion penalty* rather than overtime because overtime is generally considered as the time beyond the overall daily capacity, while we consider periodic overtime due to possible accumulation of donors within periods of the day (e.g., in the morning). Hence, rather than penalizing the overall overtime, it may be useful to penalize the periodic accumulations of donors (i.e., the overtime in each period of the day) in order to disperse them towards the underutilized parts of the day. This also compensates the higher arrival of non-booking donors in certain periods by allocating the booked donors in the others. Let us consider two examples that motivate the implementation of the periodic dispersion. In the first example, assume that no donors arrive at period $k = 1$ and that the overall service time in the other periods $k = 2, \dots, K$ exceeds the corresponding periodic capacities (i.e., $\sum_{k=2, \dots, K} c_{tk}$), while the overall system capacity ($\sum_{k=1, \dots, K} c_{tk}$) is not exceeded. We might not have daily overtime according to the classical definition, even though we observe periodic ones. Thus, focusing on the daily overtime is not accurate since additional service time is actually required to serve donors arriving from $k = 2$. In the second example, assume that the service time required in the first period $k = 1$ is higher than the corresponding capacity c_{t1} and that the service times required in the other periods are not over their periodic capacities. Even though this situation does not result in daily overtime, it is not desirable since waiting times in the first period might be high. Hence, a dispersion penalty for each period helps to both balance service times among periods and reduce waiting times.

Some additional decision variables are finally included to model the preallocation problem. The number of preallocated slots for blood type b in day t and period k is represented by a non-negative integer variable w_{tk}^b , whose sum over $k \in K$ provides x_t^b . The overall number of planned donations for blood type b at day t is y_t^b , which is given by $x_t^b + a_t^b + n_t^b$. The absolute variation of y_t^b with respect to its average value over the days t is denoted as z_t^b ; thus, the summation and the maximum of z_t^b over t are linear terms to represent the variance of y_t^b .

Sets, parameters and decision variables are summarized in Table 1. Variables are subject to the following constraints:

$$y_t^b = x_t^b + n_t^b + a_t^b, \quad \forall t \in T, b \in B \quad (1)$$

$$\sum_{\tau \in T} y_\tau^b - y_t^b |T| \leq z_t^b |T|, \quad \forall t \in T, b \in B \quad (2)$$

$$y_t^b |T| - \sum_{\tau \in T} y_\tau^b \leq z_t^b |T|, \quad \forall t \in T, b \in B \quad (3)$$

$$v \geq z_t^b, \quad \forall t \in T, b \in B \quad (4)$$

$$(1 - \varepsilon)d_b \leq \sum_{t \in T} (x_t^b + a_t^b), \quad \forall b \in B \quad (5)$$

$$\sum_{t \in T} (x_t^b + a_t^b) \leq (1 + \varepsilon)d_b, \quad \forall b \in B \quad (6)$$

Table 1

Sets, parameters and decision variables for the preallocation model.

Sets	
B	Set of blood types
T	Time horizon
K	Set of time periods in a day (same $\forall t \in T$)
Parameters	
d_b	Expected number of booked donors over T with blood type b
ε	Flexibility degree associated with d_b (same $\forall b \in B$)
a_t^b	Number of already booked donors at day t with blood type b
n_t^b	Expected number of non-booked donors at day t with blood type b
α_k	Fraction of n_t^b in period k (same $\forall t \in T$)
c_{tk}	Overall capacity of physicians (time) in period k of day t
r	Standard time required for serving a donor
R_{tk}	Time amount for serving the already booked donors in period k of day t
μ	Maximum fraction of the total dispersion penalty in a day with respect to the overall capacity in the same day
η	Maximum variation weight (for the objective function)
δ_k	Weight of the dispersion penalty in period k (same $\forall t \in T$, for the objective function)
Decision variables	
x_t^b	Number of preallocated slots for blood type b in day t
w_{tk}^b	Number of preallocated slots for blood type b in period k of day t
y_t^b	Number of planned units for blood type b in day t
z_t^b	Absolute variation of y_t^b with respect its average value over T
v	Maximum of the variations $z_t^b \forall t \in T, b \in B$
p_{tk}	Dispersion penalty in period k of day t

$$x_t^b = \sum_{k \in K} w_{tk}^b, \quad \forall t \in T, b \in B \quad (7)$$

$$r \sum_{b \in B} (w_{tk}^b + \alpha_k n_t^b) + R_{tk} \leq c_{tk} + p_{tk}, \quad \forall k \in K, t \in T \quad (8)$$

$$\sum_{k \in K} p_{tk} \leq \mu \sum_{k \in K} c_{tk}, \quad \forall t \in T \quad (9)$$

$$p_{tk} \geq 0, \quad \forall k \in K, t \in T$$

$$x_t^b, y_t^b \in \mathbb{N}, \quad \forall t \in T, b \in B$$

$$w_{tk}^b \in \mathbb{N}, \quad \forall k \in K, t \in T, b \in B$$

Constraints (1) compute the number of blood units y_t^b for each day t and blood type b . Constraints (2) and (3) calculate the absolute variation z_t^b between y_t^b and its average value over T , and constraints (4) compute the maximum of such absolute variations. Constraints (5) and (6) force the total number of slots of type b to be around d_b , with tolerance ε ; obviously, the number of slots is an integer number, so that the effect of these constraints is to bound $\sum_{t \in T} (x_t^b + a_t^b)$ between $\lceil (1 - \varepsilon)d_b \rceil$ and $\lfloor (1 + \varepsilon)d_b \rfloor$. Constraints (7) calculate, for each blood type b , the total number of preallocated slots x_t^b in day t based on the w_{tk}^b amounts. Constraints (8) calculate the dispersion penalty p_{tk} based on service times and physicians' capacities. Constraints (9) limit the total dispersion penalty in a day to be at most a given fraction of the overall capacity in the same day, where μ is such fraction.

In this formulation, we assume that all arriving donors make a donation, that all booked donors show up at the right period and day, and we do not consider different types of donations other than the whole blood donation (e.g., apheresis).

The primary objective of the model is to balance the production of each blood type b among the days, which corresponds to obtaining low z_t^b values. Moreover, the secondary goal is to minimize the dispersion penalties p_{tk} , where the penalty of each period $k \in K$ is weighted through a specific parameter δ_k . Hence, the following objective function is considered, which is composed by three

terms:

$$\min \left\{ \sum_{b \in B} \sum_{t \in T} z_t^b + \eta \nu |T| |B| + \sum_{t \in T} \sum_{k \in K} \delta_k D_{tk} \right\} \quad (10)$$

The first two terms (named OF1 and OF2, respectively) balance the production among days by reducing the absolute variations z_t^b ; OF1 minimizes the total absolute variation with respect to the average production, while OF2 minimizes the maximum absolute variation among all days and all blood types. The third term (named OF3) minimizes the total weighted dispersion penalty. The objective function may contain all three terms, as reported in (10), or alternatively it may include only one or two of them. If OF2 is neglected, constraints (4) can be removed from the model, while constraints (8) can be removed if OF3 is not considered.

Let us focus on the first two terms OF1 and OF2, which both aim at balancing the production. η is a positive parameter that represents the relative weight of the maximum absolute variation with respect to the total one: a low value of η favors the total variation, whereas higher values favor controlling the maximum variation. Decision variable ν is multiplied by $|T|$ and $|B|$ to obtain, with $\eta = 1$, the same order of magnitude for the two terms. It is common in optimization problems that both the summation and the maximum of a set of decision variables are optimized. But, in our case, these two terms may lead to allocate a different number

of slots x_t^b , since y_t^b is given by $x_t^b + n_t^b + a_t^b$ and the summation $\sum_{t \in T} x_t^b + a_t^b$ is not constrained to a value but to a range, due to (5) and (6). On the contrary, in several other problems, the overall amount is generally fixed and just differently allocated. Further details will be provided in Section 5.

We finally underline that our framework assigns a day t and a period k to each donor, and we can tune the granularity of the assignments based on the number K of periods in a day. For example, with $K = 3$, the donor is addressed to a period that is obviously longer than the actual duration of the slots; thus, for a practical application, the appointment can be further refined considering a real scheduling within such period. Alternatively, with higher values of K , the length of the periods could be comparable with that of slots and the assigned period could also refer to the scheduled time.

4.2. Prioritization policy for the online allocation of slots

The goal of the prioritization policy is to decide the best preallocated slot to propose when a donor calls to make a reservation. However, proposing only one day to the donor is not enough because the donor may have other constraints and could not accept the proposal. Thus, it is preferable to propose a list of possible days t and periods k , and let the donor choose among them. This might increase the donation frequency and the perceived usefulness of the donation from the donor. Hence, the goal of this second phase is to assign a score to each slot of the donor's blood type, such that the slots can be proposed one by one to the donor in a decreasing order of score until a slot is accepted. This is a good compromise between donor's needs (propose several alternatives) and production needs (propose the best alternative).

Basically, there are two points behind the prioritization of the slots and the assignment of the score: to fill the first available day and to keep the flexibility of the reservation system. The first point requires assigning the donor in the first available day according to his/her blood type. In fact, keeping the first available slots empty may negatively affect the system if no further donors of the same blood type will ask for reserving a donation, because such slots will remain empty. The second point requires not to fill all of the preassigned slots of a day; otherwise, the range of choice for the next calling donor is reduced. Hence, flexibility means to assign

donors in the day with the highest number of preallocated slots still available. Both points are taken into account while assigning scores, each one weighted by a value. The score S_{tkb} of slots w_{tk}^b is computed ($\forall t, k, b$) by the following linear formula:

$$S_{tkb} = \lambda_f w_{tk}^b - \lambda_d t \quad (11)$$

where t represents, according to the MILP model, the day in the time horizon, starting from the current one in which reservations are arriving ($t = 1$).

The first term generates higher scores for higher values of w_{tk}^b , i.e., when the flexibility remains higher if the donor of blood type b is allocated to t and k ; the second term, due to the minus sign, generates higher scores when the donor is allocated to as low as possible values of t (i.e., to a closer day). λ_f is the weight of the flexibility term, while λ_d is the weight of the early allocation term.

Preallocated time slots are thus sorted and proposed one by one in a decreasing order of score. If the donor accepts the first proposed slot, this maximizes the goals of the system. In any case, we remark that every request for reservation is accepted: if no slots are available in the donor's suitable days, an additional slot is forced with respect of the preallocated ones.

Each time a reservation is made, the corresponding value x_t^b is reduced by 1 in view of the next calls, in order to respect the capacity. Moreover, before rerunning the preallocation model, all a_t^b values are updated with the new reservations.

Alternative scoring schemes have been also considered. However, the one we propose in this work includes the two priorities highlighted by the staff of AVIS Milan (i.e., filling the first available day and keeping the flexibility of the reservation system) which are also common to several other blood collection centers.

When a donor calls to make a reservation, it might happen that either no more slots are available for his/her blood type, or slots are available only in days that are not accepted by the donor. In these cases, the donation slot is chosen considering the slots still available from the other blood types. In addition, in case no existing slots are accepted by the donor, a new slot is added to the plan. In this way, no donor is rejected. This choice may create an unbalancing in the plan; however, due to the cyclic approach (Fig. 2(b)), this local unbalancing is quickly reabsorbed. Anyway, we would like to mention that this situation is extremely rare in the case of well dimensioned d_b . If this event happens, this means that the BD collection center has to revise the values of parameters d_b .

5. Complexity and valid inequalities

In this section, we analyze some particular cases of the preallocation problem and we prove that they are polynomially solvable (Section 5.1). Then, we consider a generalization of the problem (Section 5.2), and we derive some valid inequalities (Section 5.3).

5.1. Subproblems

Let us first consider a special case with only OF1 in the objective function, one blood type b^* ($|B| = 1$), a constant number of non-booked donors ($n_t^{b^*} = \bar{n}^{b^*}$, $\forall t$), no preallocated slots ($a_t^{b^*} = 0$, $\forall t$), and infinite capacities ($c_{tk} \rightarrow \infty$, $\forall t, k$). We denote it as *Single Blood Type under OF1 objective* (SBT-OF1) problem.

Definition 1. Given a time horizon T and two values d_{min} and d_{max} , the SBT-OF1 problem consists of finding an integer value $N \in [d_{min}, d_{max}]$ and an allocation of slots to days $x_t^{b^*}$ ($t \in [1, \dots, |T|]$) such that $\sum_{t \in T} x_t^{b^*} = N$ and $\sum_{t \in T} |x_t^{b^*} - \frac{N}{T}|$ is minimized.

We observe that $d_{min} = \lceil (1 - \varepsilon) d_b^* \rceil$ and $d_{max} = \lfloor (1 + \varepsilon) d_b^* \rfloor$ because of (5) and (6).

Proposition 2. *The SBT-OF1 problem can be solved in polynomial time.*

Proof. Let us consider two cases:

- (a) $\exists N^* \in [d_{min}, d_{max}] : N^* = \alpha|T|$ with α integer;
(b) there is no such value, i.e., $N = \alpha|T| + k$, with and $0 < k < |T|$.

In case *a*, the optimal solution is obtained by assigning α slots to each day, thus obtaining an objective function equal to zero, which cannot be improved as every day has precisely the same number of donations.

In case *b*, we first show that, given two values for k and N , with $N = \alpha|T| + k$, the best way to assign slots to days is to assign $\alpha + 1$ slots to k days and α slots to $|T| - k$ days. In fact, any change of one slot with respect to this assignment would increase the objective function. Let us consider the three possible cases:

1. We move one slot from one day with α assigned slots to another day with α assigned slots. The allocation is modified as follows:

- in one day we reduce the number of slots $\alpha \rightarrow \alpha - 1$: the corresponding difference in the objective function is 1;
- in one day we increase the number of slots $\alpha \rightarrow \alpha + 1$: the corresponding difference in the objective function is $1 - \frac{2k}{|T|}$.

As $1 - \frac{2k}{|T|} < 1$ on the overall the objective function increases.

2. We move one slot from one day with α assigned slots to another day with $\alpha + 1$ assigned slots. The allocation is modified as follows:

- in one day we reduce the number of slots $\alpha \rightarrow \alpha - 1$: the corresponding difference in the objective function is 1;
- in one day we increase the number of slots $\alpha + 1 \rightarrow \alpha + 2$: the corresponding difference in the objective function is 1.

On the overall the objective function increases by 2.

3. We move one slot from one day with $\alpha + 1$ assigned slots to another day with assigned $\alpha + 1$ slots. The allocation is modified as follows:

- in one day we reduce the number of slots $\alpha + 1 \rightarrow \alpha$: the corresponding difference in the objective function is $\frac{2k}{|T|} - 1$;
- in one day we increase the number of slots $\alpha + 1 \rightarrow \alpha + 2$: the corresponding difference in the objective function is 1.

As $1 > \frac{2k}{|T|} - 1$ on the overall the objective function increases.

Moving one slot from one day with α assigned slots to another day with assigned $\alpha + 1$ slots is an equivalent solution.

In this best case, the objective function is:

$$\sum_{t \in T} z_t^{b*} = \sum_{t \in T} \left| x_t^{b*} - \frac{N}{|T|} \right| = k \left(\alpha + 1 - \alpha - \frac{k}{|T|} \right) + (|T| - k) \left(\alpha + \frac{k}{|T|} - \alpha \right) = 2k \left(1 - \frac{k}{|T|} \right)$$

Thus we aim at finding $k^* \in [k_{min}, k_{max}]$, where $k_{min} = d_{min} - \alpha|T|$ and $k_{max} = d_{max} - \alpha|T|$ such that

$$2k \left(1 - \frac{k}{|T|} \right) \quad (12)$$

is minimized. Function (12) is a concave parabola, with vertex in $\frac{|T|}{2}$ and equal to 0 for $k = 0$ and $k = |T|$. In order to minimize it, we set k^* as follows:

$$k^* = \begin{cases} k_{min} & \text{if } \frac{|T|}{2} - k_{min} > k_{max} - \frac{|T|}{2} \\ k_{max} & \text{if } \frac{|T|}{2} - k_{min} < k_{max} - \frac{|T|}{2} \\ \text{indifferently } k_{min} \text{ or } k_{max} & \text{if } \frac{|T|}{2} - k_{min} = k_{max} - \frac{|T|}{2} \end{cases} \quad (13)$$

For both cases *a* and *b* the optimal allocation of slots to days can be computed in polynomial time.

Remark 3. Let us denote with SBT-OF2 a version of SBT-OF1 problem where objective function OF2 is considered instead of OF1. In

this case the objective function to be minimized is

$$v = \max \{ z_t^{b*}, t \in T \} = \begin{cases} 0 & k = \{0; |T|\} \\ \max \left\{ 1 - \frac{k}{|T|}; \frac{k}{|T|} \right\} & k \in [1; |T| - 1]. \end{cases} \quad (14)$$

which assumes a null value in $N = 0, |T|$, while it is a V-shaped function with minimum value 0.5 in $N = \frac{|T|}{2}$ for $k \in [1; |T| - 1]$.

Thus, SBT-OF2 can be solved in polynomial time.

The flexibility ε is responsible of the different behaviors between OF1 and OF2 in terms of allocated x_t^{b*} . The value chosen in (13) is in the farthest point from the maximum of the parabola; thus, OF1 allocates a number of slots as close as possible to a multiple of $|T|$. On the contrary, if a perfect balancing is not possible, the minimum of (14) is obtained by allocating a number of slots as close as possible to the intermediate value between two consecutive multiples of $|T|$.

Let us consider a version of the problem with only one blood type b^* ($|B| = 1$), a constant number of non-booked donors ($n_t^{b*} = \bar{n}^{b*}, \forall t$), and infinite capacities ($c_{tk} \rightarrow \infty, \forall t, k$). But, now, let us consider some preallocated slots $a_t^{b*} \geq 0$ such that $a_t^{b*} \leq \xi_t^{b*}$, where ξ_t^{b*} denotes the optimal value of x_t^{b*} in the corresponding problem with $a_t^{b*} = 0, \forall t$. We denote the subproblem as SBT-P, regardless of the considered objective function.

Remark 4. SBT-P can be solved in polynomial time.

In fact, the same procedure used to compute the optimal value for SBT-OF1 and SBT-OF2 can be applied, as $\sum_{t \in T} (x_t^{b*} + a_t^{b*})$ is bound to around d_b . Indeed, the number of preallocated slots x_t^{b*} is computed as $\xi_t^{b*} - a_t^{b*}$.

Let us consider a version of SBT-OF1 or SBT-OF2 where more than one blood type, i.e., $|B| > 1$ is considered. We denote the subproblem as MBT problem, regardless of the objective function considered.

Remark 5. MBT is polynomially solvable.

In fact, thanks to the unlimited capacity, the problem can be decomposed into several SBT problems one for each blood type.

5.2. Generalized version

We remove now the assumption of the infinite capacities, meaning both to consider a maximum amount by means of fraction μ and to pay for overtime in OF3 due to penalties δ_k . By removing the assumption of infinite capacity, the slots of the different blood types cannot be preallocated individually, and the problem cannot be decomposed anymore. Indeed, the best balancing obtained with infinite capacities could not be achieved: while trying to improve the balancing, the overall dispersion penalty in OF3 could be more expensive than the corresponding reduction of OF1 and/or OF2, so that the system could prefer more unbalanced solutions.

A complexity proof for this case can be derived in a generalized version of the problem. The generalization assumes that the donors are divided in G classes (depending, e.g., on their age or health conditions), each one requiring a different service time r_g ($g = 1, \dots, G$). Moreover, also d_b and n_t^b depend on the class, i.e., they are redefined as d_{bg} and n_t^{bg} .

Let us refer to this version of the problem as G-BTA (Generalized blood type assignment). The G-BTA can be proved to be NP-complete.

In fact, it can be reduced from the Bin Packing problem. In its decisional form, the Bin Packing problem asks whether κ bins, each one with capacity B , can contain a set of items I , each with

its own weight w_i . An instance of G-BTA representing the instance of Bin Packing can be built as follows:

- one day with κ time periods, each with the same capacity B , is considered;
- one blood type is considered and one donor group is generated for each item, whose visit time is equal to the item weight. ϵ is set equal to 0 and d_b^g equal to 1. No assigned slots nor walk-in donors are considered;
- we focus only on the penalty objective function.

If there exists a solution of G-BTA with null value of dispersion penalty, then there exists a solution of the Bin Packing problem with value κ .

5.3. Lower bounds

In case of unavoidable unbalancing, it can be time consuming to close the gap between the integer solution and the continuous relaxation in commercial solvers (e.g., CPLEX solver). Indeed, the continuous relaxation splits N among the days with fractional allocations, whereas the actual integer solution does not. Thus, the branch-and-bound procedure continues, systematically generating sub problems to analyze and discarding those that do not improve the objective lower bound. Valid inequalities can be added to reduce computational times, i.e., additional cuts that reduce the admissible region of only the continuous relaxation by bounding the values of OF1 and OF2.

The above described problems can be used to derive some lower bounds on the value of OF1 and OF2. In particular, in case of constant n_t^b , we bound OF1 and OF2 with the best possible balancing obtained by (12) and (14), respectively, in a closed analytical form.

The lowest value of OF1 for a given blood type b^* is given by (see SBT-OF1):

$$2 \min \left\{ k_{\min} \left(1 - \frac{k_{\min}}{|T|} \right); k_{\max} \left(1 - \frac{k_{\max}}{|T|} \right) \right\}$$

Its summation over the blood types, assuming a null value for those types where a perfect balancing is possible, gives the lower bound LB_{OF1} . Hence, the following lower bound constraint LB1 can be added to the model:

$$\sum_{b \in B} \sum_{t \in T} z_t^b \geq LB_{OF1} \quad (15)$$

We remark that LB_{OF1} is computed from the available data before the model is run and, thus, it is another model parameter.

The lowest value of OF2 for a given blood type b^* is given by (see SBT-OF2):

$$\begin{cases} 0 & k_{\min} = 0 \text{ or } k_{\max} = |T| \\ 1 - \frac{k_{\max}}{|T|} & k_{\min} > 0 \text{ and } k_{\max} \leq \frac{|T|}{2} \\ \frac{k_{\min}}{|T|} & k_{\min} \geq \frac{|T|}{2} \text{ and } k_{\max} < |T| \\ \frac{1}{2} & 0 < k_{\min} < \frac{|T|}{2} \text{ and } \frac{|T|}{2} < k_{\max} < |T| \end{cases}$$

Then, the highest of the values among the blood types b gives the lower bound LB_{OF2} . Hence, the following lower bound constraint LB2 can be added to the model:

$$v \geq LB_{OF2} \quad (16)$$

We remark that also LB_{OF2} is computed from the available data and it is another model parameter.

We underline that, due to the opposite behaviors of OF1 and OF2, the lower bounds LB_{OF1} and LB_{OF2} cannot be reached at the same time (when greater than 0), and the lower bound of their summation is for sure higher than $LB_{OF1} + \eta|T||B|LB_{OF2}$. Thus, OF1 does not make OF2 useless and vice versa.

6. Computational tests

In this section, we first present the computational tests to analyze the behavior of the preallocation model, considering the impact of the modeling assumptions and the related parameters (Section 6.1). Then, we evaluate the performance of the entire approach (preallocation model and prioritization policy) over a period of time with realistic instances derived from the AVIS Milan case (Section 6.2) and randomly generated instances (Section 6.3). We evaluate in Section 6.1 several parametric settings of the preallocation model and, from the analyses, we derive some alternatives for the following tests in Sections 6.2 and 6.3.

Further experiments to test computational aspects of the preallocation model and additional figures related to the entire approach are also presented in the *Supplementary material*.

The preallocation model is implemented in IBM ILOG OPL and solved via CPLEX 12. The entire approach is implemented in Microsoft Visual Basic, and the developed solution integrates the data and the prioritization policy with the input and the output of the OPL model. All experiments are run on a Windows Machine installed on a server with CPU Intel® Core™ i3, 2.40 gigahertz, and 12 gigabytes of dedicated RAM.

Instances used for Sections 6.2 and 6.3 are available online on Mendeley (DOI <http://10.17632/sd8dpcwgg8.2>).

6.1. Modeling assumptions and parameters

We test our modeling assumptions (i.e., the impact of d_b flexibility through ϵ , dispersion penalty weights δ_k , and maximum fraction μ) and the behavior of the model in response to different parameter values. Tests are conducted with two classes of instances, namely, class A and B; a time limit of 5400 seconds and a memory limit of 3 gigabytes have been imposed in all experiments.

Instances of class A (to test ϵ and p_{tk}) are divided in two groups, denoted by A.1 and A.2, respectively, where the differences between the groups refer to the number of non-booked donors (n_t^b) for each day and blood type. Group A.1 includes the *balanced* instances, in which each n_t^b is randomly generated close to a nominal value, and the summation $\sum_t n_t^b$ over the days is the same for each blood type b . Group A.2 includes the *unbalanced* instances, in which the summation $\sum_t n_t^b$ is again the same for each blood type b as in Group A.1. But, in this group, an unbalancing among the days is included by considering higher values in the first days of the planning horizon and lower values in the last days. The goal is to replicate practical cases, where there can be more non-booked donors than usual in some days, especially after holiday periods.

In both groups we further consider three levels for the fraction of non-booked donors with respect to the total number of donors: Null (N), Medium (M), and High (H). The list of the instances is reported in Table 2. Note that in all cases, for the sake of simplicity, booked donors are not considered ($a_t^b = 0, \forall t, b$). All instances are generated by considering 8 blood types ($|B| = 8$), 7 days of time horizon ($|T| = 7$) with 3 periods ($|K| = 3$), and capacities c_{tk} equal to 240, 300 and 180 minutes for $k = 1, 2, 3$.

Table 2
Summary of the instances in Group A.

Group	Non-booked level	$d_b, \forall b$	$\sum_t n_t^b, \forall b$
A.1	Null (N)	51	0
	Medium (M)	34	17
	High (H)	17	34
A.2	Null (N)	51	0
	Medium (M)	34	17
	High (H)	17	34

Table 3
Impact of ε and δ_k on the objective function terms for Group A.1. * and • indicate that the run is terminated because the memory limit or the time limit has been reached, respectively; the maximum optimality gap over these cases is 2.69%.

Non-booked		$\delta = [8 \ 6 \ 3]$			$\delta = [0.8 \ 0.6 \ 0.3]$			$\delta = [0.08 \ 0.06 \ 0.03]$			$\delta = [0.008 \ 0.006 \ 0.003]$		
level	ε	OF1	OF2	OF3	OF1	OF2	OF3	OF1	OF2	OF3	OF1	OF2	OF3
Null (N)	0.00	22.86	40.00	3240.00	22.86	40.00	324.00	22.86	40.00	32.40	22.86*	40.00*	3.24*
	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	0.50	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	0.75	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Medium (M)	0.00	22.86	40.00	3249.00	22.86	40.00	324.90	22.86	40.00	32.49	22.86	40.00	3.25
	0.25	13.71	48.00	369.00	13.71	48.00	36.90	0.00	0.00	25.29	0.00	0.00	2.53
	0.50	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	0.75	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
High (H)	0.00	22.86	40.00	5058.00	22.86	40.00	505.80	22.86•	40.00•	50.58•	22.86*	40.00*	5.06*
	0.25	22.86	40.00	3618.00	22.86*	40.00*	361.80*	0.00	0.00	43.38	0.00	0.00	4.34
	0.50	27.43*	32.00*	2898.00*	27.43*	32.00*	289.80*	0.00	0.00	43.38	0.00	0.00	4.34
	0.75	0.00	0.00	2898.00	0.00	0.00	289.80	0.00	0.00	28.98	0.00	0.00	2.90
	1.00	0.00	0.00	2898.00	0.00	0.00	289.80	0.00	0.00	28.98	0.00	0.00	2.90

Table 4
Impact of ε and δ_k on the objective function terms for Group A.2. * and • indicate that the run is terminated because the memory limit or the time limit has been reached, respectively; the maximum optimality gap over these cases is 13.63%.

Non-booked		$\delta = [8 \ 6 \ 3]$			$\delta = [0.8 \ 0.6 \ 0.3]$			$\delta = [0.08 \ 0.06 \ 0.03]$			$\delta = [0.008 \ 0.006 \ 0.003]$		
level	ε	OF1	OF2	OF3	OF1	OF2	OF3	OF1	OF2	OF3	OF1	OF2	OF3
Null (N)	0.00	22.86	40.00	3240.00	22.86	40.00	324.00	22.86	40.00	32.40	22.86*	40.00*	3.24*
	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	0.50	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	0.75	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Medium (M)	0.00	22.86	40.00	3666.00	22.86	40.00	366.60	22.86	40.00	36.66	22.86	40.00	3.67
	0.25	13.71	48.00	786.00	13.71	48.00	78.60	0.00	0.00	29.46	0.00	0.00	2.94
	0.50	0.00	0.00	480.00	0.00	0.00	48.00	0.00	0.00	4.80	0.00	0.00	0.48
	0.75	0.00	0.00	480.00	0.00	0.00	48.00	0.00	0.00	4.80	0.00	0.00	0.48
	1.00	0.00	0.00	480.00	0.00	0.00	48.00	0.00	0.00	4.80	0.00	0.00	0.48
High (H)	0.00	54.86	152.00	6402.00	54.86	152.00	640.20	54.86	152.00	64.02	54.86	152.00	6.40
	0.25	69.14*	184.00*	5304.00*	68.57	176.00	533.10	41.14•	120.00•	78.42•	41.14*	120.00*	7.84*
	0.50	69.14*	184.00*	5304.00*	68.57	176.00	533.10	27.43	96.00	89.22	34.29	88.00	9.28
	0.75	69.14*	184.00*	5304.00*	68.57	176.00	533.10	16.00	56.00	107.22	16.00	56.00	10.72
	1.00	69.14*	184.00*	5304.00*	68.57	176.00	533.10	13.71	48.00	110.82	27.43*	32.00*	11.80*

respectively, in all days t . Service durations are assumed to be 15 minutes ($r = 15$) and α_k fractions are considered equal to 0.5, 0.3 and 0.2 for $k = 1, 2, 3$, respectively.

Several experiments are conducted by varying ε and δ_k values, to test d_b flexibility and the weights of the dispersion penalty with respect to the production balancing (OF1 and OF2). For each instance group and level of non-booked donors, 20 different combinations of ε and δ_k values are tested. In all these cases, we have considered the entire objective function (OF1 + OF2 + OF3) while setting $\eta = 1$. Moreover, as we want to exclude constraints (9) in the analysis, we assume a high μ value equal to the 100%, which is never reached in the considered instances.

Results are reported in Tables 3 and 4. It can be observed that, for higher $\delta = [\delta_1 \ \delta_2 \ \delta_3]$ values (i.e., $\delta = [8 \ 6 \ 3]$ and $\delta = [0.8 \ 0.6 \ 0.3]$), the dispersion penalty term OF3 is privileged, with consequent higher OF1 and OF2 values (meaning an unbalanced system) for lower ε values. For higher ε values, as expected, the system remains balanced also with high δ_k values, because of the flexibility given by the larger range around d_b . On the other hand, lower δ_k values (i.e., $\delta = [0.08 \ 0.06 \ 0.03]$ and $\delta = [0.008 \ 0.006 \ 0.003]$) result in completely balanced solutions as long as $\varepsilon > 0$, which also show decreasing OF3 values while increasing ε . Only for Level H of Group A.2, the high unbalanced arrival of non-booked donors always prevents from a perfect balancing (OF1 $\neq 0$ and OF2 $\neq 0$, $\forall \varepsilon$) and determines increased OF3 values

with ε , because the system tries to compensate the unbalancing by adding slots.

To confirm these outcomes, we have also conducted additional tests on other instances (e.g., with $a_t^b > 0$ and longer time horizons $|T|$). The results are very similar and confirm the observations and the conclusions we drawn above, which are therefore generalizable. However, for lack of space, these additional outcomes are not detailed in the paper.

Fig. 4 shows the ratio between the number of allocated slots ($\sum_t \sum_b x_t^b$) and the total number of expected donors ($\sum_b d_b$) as a function of ε for both groups and all levels of non-booked donors (for $\delta = [0.08 \ 0.06 \ 0.03]$). It can be seen that, as expected, the number of allocated slots decreases while ε increases, except in level H of Group A.2. Thus, better balancing and lower dispersion penalties for higher ε values are observed due to the reduced number of assigned slots. On the contrary, as for level H of Group A.2, the model allocates more slots to partially compensate the unbalancing given by the high and unbalanced amount of non-booked donors. Anyway, as mentioned in Section 4.1 too high values of ε are not of interest for a practical application, meaning no information about the d_b parameters.

Other analyses are conducted to investigate how the dispersion penalty is divided among periods $k \in K$ (Fig. 5), how booked and non-booked donors are scheduled in a day (Fig. 6), and how many units per day are produced while trying to balance the production (Fig. 7). All figures refer to the case with all terms in

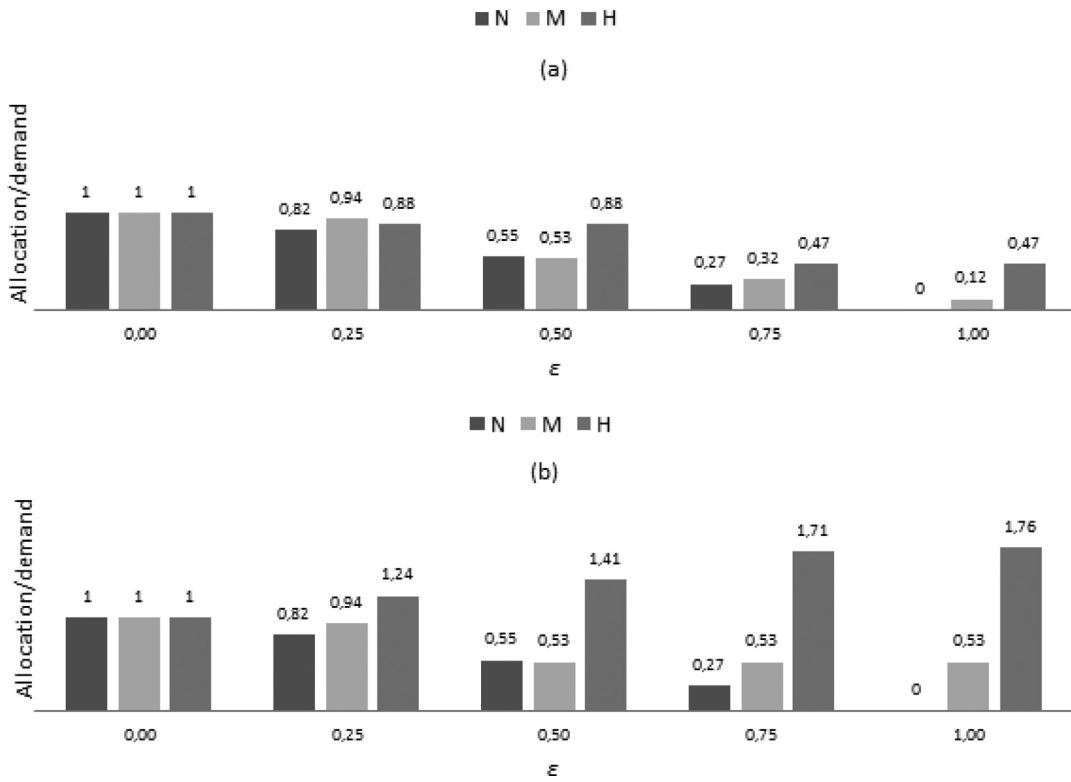


Fig. 4. Allocated slots ($\sum_t \sum_b x_t^b$) over demand ($\sum_b d_b$) for 5 different ϵ values and 3 non-booked donor levels: null (N), medium (M) and high (H). (a) refers to Group A.1 and (b) to Group A.2.

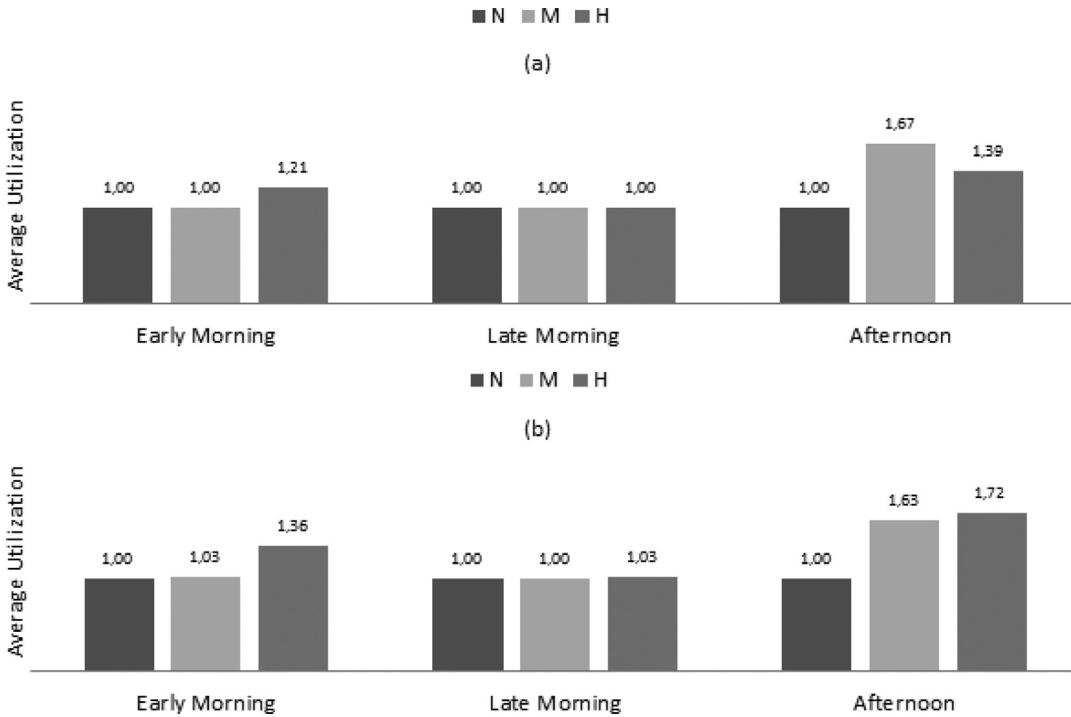


Fig. 5. Average utilization for 3 different periods, namely *early morning* ($k = 1$), *late morning* ($k = 2$), and *afternoon* ($k = 3$). (a) refers to Group A.1 and (b) to Group A.2, both including the 3 levels of non-booked donors.

the objective function (OF1, OF2 and OF3), and with parameters $\delta = [0.08 \ 0.06 \ 0.03]$, $\eta = 1$ and $\epsilon = 0.25$.

Fig. 5 shows the average utilization among days t for each period k , where utilization in t and k is given by $(r \sum_{b \in B} (w_{tk}^b + \alpha_k n_t^b) + R_{tk}) / c_{tk}$, and for the 3 levels of non-booked donors (N, M and H). In general, results show the possibility of shifting

the donor accumulation to the period k with the lowest weight δ_k . However, for level H, overutilization is also present in the most weighted period of the day (i.e., $k = 1$ in our case) because of the high and unbalanced number of non-booked donors, which are not controllable.

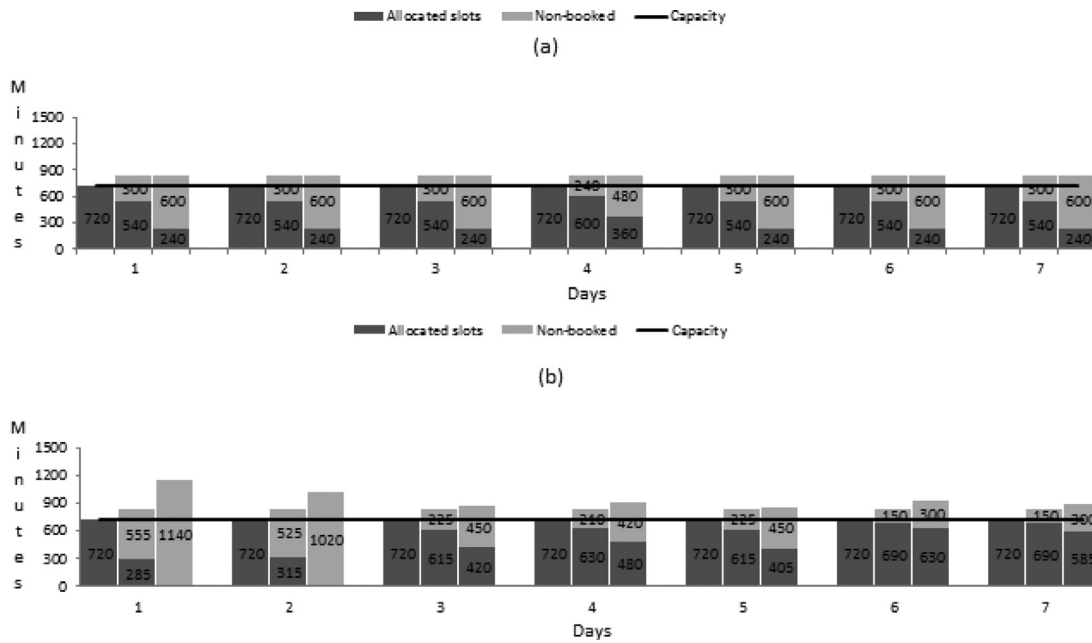


Fig. 6. Daily workload for the 3 levels of non-booked donor: N (first column in each day), M (second column in each day), and H (third column in each day). (a) refers to Group A.1 and (b) to Group A.2.

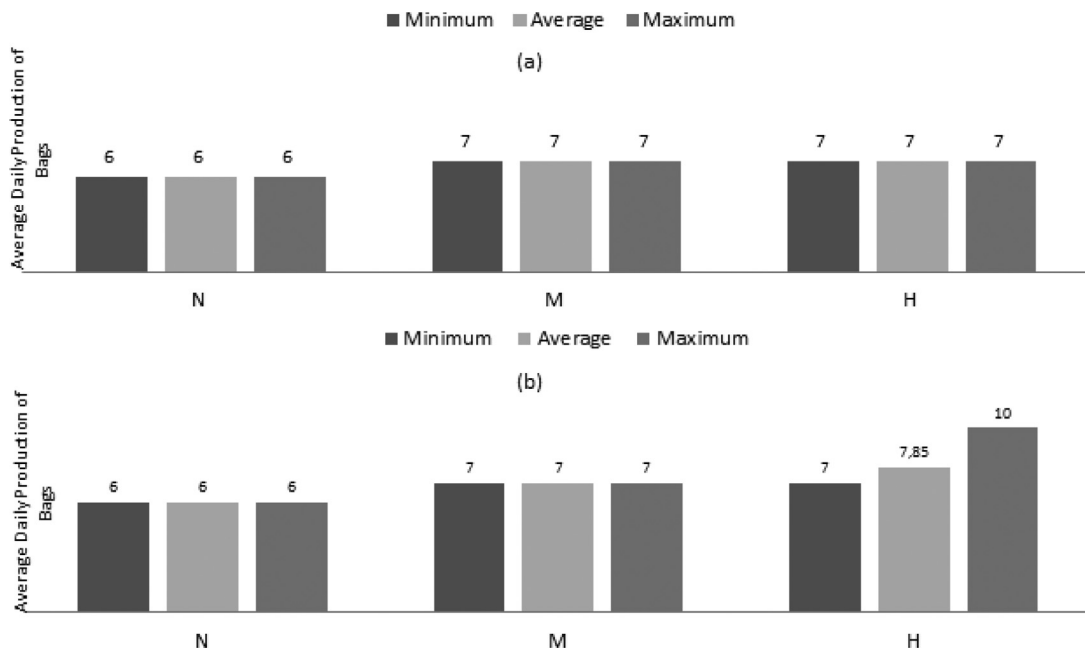


Fig. 7. Minimum, average and maximum daily production for a blood type (same values for all types) for the 3 levels of non-booked donors: null (N), medium (M) and high (H). (a) refers to Group A.1 and (b) to Group A.2.

Fig. 6 shows the daily workload (compared with the capacity) for each day t . It can be seen that the model equally divides the total workload among days, as production balancing is the primary objective. Moreover, equal proportions of booked and non-booked donors are found in all days for Group A.1, while the proportions vary from day to day in Group A.2. This means that, in the presence of balanced non-booked donors, the system equally allocates slots in the days to keep the situation balanced, while slots are preallocated to compensate the unbalanced input in the presence of unbalanced non-booked donors.

Lastly, Fig. 7 shows the minimum, average and maximum daily production of blood units among days t for a given blood type b (values are the same for all blood types, as the same d_b values

are used $\forall b$). The model perfectly balances the daily production; the only difference is again due to the unbalanced number of non-booked donors that affects the production in the H case of Group A.2.

It can be seen from the analyses that the amount of non-booked donors, in the presence of unbalanced arrivals, has a great impact on the system, both in terms of utilization dispersion and balancing (see in particular level H of Group A.2). However, with an appropriate set of parameters, the model is able to find a good trade-off between production balancing and accumulation reduction also in this case. Thus, the decision maker can choose the preferred set of parameters based on his/her priorities and the features of the blood collection center. Another parameter with a high

Table 5
Impact of μ , δ_k and c_{tk} on OF3 for Group B.1 (a) and B.2 (b); *inf.* indicates infeasibility.

$\Sigma_k c_{tk}$		$\delta = [0.095 \ 0.05 \ 0.005]$				$\delta = [0.08 \ 0.06 \ 0.03]$				$\delta = [0.055 \ 0.05 \ 0.045]$			
$\forall t$	μ	$\Sigma_t p_{t1}$	$\Sigma_t p_{t2}$	$\Sigma_t p_{t3}$	OF3	$\Sigma_t p_{t1}$	$\Sigma_t p_{t2}$	$\Sigma_t p_{t3}$	OF3	$\Sigma_t p_{t1}$	$\Sigma_t p_{t2}$	$\Sigma_t p_{t3}$	OF3
720	0.00	inf.	inf.	inf.	inf.	inf.	inf.	inf.	inf.	inf.	inf.	inf.	inf.
	0.50	0.00	0.00	843.00	4.22	0.00	0.00	843.00	25.29	0.00	12.00	828.00	37.86
	1.00	0.00	0.00	843.00	4.22	0.00	0.00	843.00	25.29	0.00	12.00	828.00	37.86
810	0.00	0.00	0.00	0.00	1.07	0.00	0.00	0.00	6.39	0.00	0.00	0.00	9.51
	0.50	0.00	0.00	213.00	1.07	0.00	0.00	213.00	6.39	0.00	12.00	198.00	9.51
	1.00	0.00	0.00	213.00	1.07	0.00	0.00	213.00	6.39	0.00	12.00	198.00	9.51

(a)

$\Sigma_k c_{tk}$		$\delta = [0.095 \ 0.05 \ 0.005]$				$\delta = [0.08 \ 0.06 \ 0.03]$				$\delta = [0.055 \ 0.05 \ 0.045]$			
$\forall t$	μ	$\Sigma_t p_{t1}$	$\Sigma_t p_{t2}$	$\Sigma_t p_{t3}$	OF3	$\Sigma_t p_{t1}$	$\Sigma_t p_{t2}$	$\Sigma_t p_{t3}$	OF3	$\Sigma_t p_{t1}$	$\Sigma_t p_{t2}$	$\Sigma_t p_{t3}$	OF3
720	0.00	inf.	inf.	inf.	inf.	inf.	inf.	inf.	inf.	inf.	inf.	inf.	inf.
	0.50	60.00	0.00	843.00	9.22	60.00	12.00	798.00	29.46	75.00	27.00	738.00	38.69
	1.00	60.00	1.50	828.00	9.22	60.00	12.00	798.00	29.46	75.00	27.00	738.00	38.69
810	0.00	inf.	inf.	inf.	inf.	inf.	inf.	inf.	inf.	inf.	inf.	inf.	inf.
	0.50	7.50	1.50	258.00	2.08	7.50	27.00	198.00	8.16	30.00	27.00	153.00	9.89
	1.00	7.50	0.00	273.00	2.08	7.50	27.00	198.00	8.16	30.00	27.00	153.00	9.89

(b)

impact is ε , which models the flexibility degree associated with d_b . As shown, high values of ε may deteriorate the quality of the solution and, in particular, reduce the amount of produced units. Thus, the decision maker should accurately set this value not to constrain the solution on a number of donors different from the actual one, but also not to reduce the production without a real motivation coming from the data.

Instances of class B (to test μ and its relationship with c_{tk} and δ_k) are divided in two groups, namely, B.1 and B.2. Instances of Group B.1 are derived from the *balanced* Group A.1, with non-booked level M and $\varepsilon = 0.25$, while instances of Group B.2 from the *unbalanced* Group A.2, again with non-booked level M and $\varepsilon = 0.25$. The alternative values for the parameters in both B.1 and B.2 are reported below:

- μ : equal to either 0, 0.5, or 1;
- $\mathbf{c}_t = [c_{t1} \ c_{t2} \ c_{t3}]$: equal to either [240 300 180] $\forall t$ (with $\sum_k c_{tk} = 720$), or [270 330 210] $\forall t$ (with $\sum_k c_{tk} = 810$);
- $\delta = [\delta_1 \ \delta_2 \ \delta_3]$: equal to either [0.095 0.05 0.005], [0.08 0.06 0.03], or [0.055 0.05 0.045].

Outcomes are reported in Table 5. All tests have been solved to optimality and the optimal solutions always show OF1=OF2=0 in all cases. Results show that the preallocation model successfully takes into account the dispersion of donors, i.e., it first allocates slots to fill all periodic capacities c_{tk} and then allocates slots in the periods with lower δ_k penalty values. Moreover, as expected, infeasibilities can be removed by increasing the parameter μ . Finally, we can observe that, in the *balanced* Group B.1, the slots are assigned in such a way to first saturate the capacity of the period with the lowest δ_k ($k = 3$ in our case) and then the capacity of the period with the second last δ_k ($k = 2$ in our case). On the contrary, in the *unbalanced* Group B.2, slots above the capacity are exploited in $k = 1$ and $k = 2$ at the same time.

6.2. Entire approach (AVIS Milan case)

We test the effectiveness of the entire approach on a realistic instance derived from AVIS Milan case.

Experiments are conducted with a rolling approach; the preallocation model is run, at each rolling day, considering the previously assigned slots (a_t^b), and then the newly arriving calls for reservation are addressed to one of the preallocated slots x_t^b . The corresponding value x_t^b is reduced by 1 after each reservation is made; moreover, a_t^b values are updated at the end of the day with

the new reservations, and the day t is shifted to $t + 1$. Then, the two phases are repeated, and so forth. The considered rolling period consists of 200 days, and the preallocation model is run at each rolling day with a planning period of $|T| = 28$ horizon days. At the first rolling day, we start from an empty condition without booked donors ($a_t^b = 0, \forall t, b$).

The number of donors at each rolling day and their blood types are directly taken from the historical data of AVIS Milan, considering the whole blood donations over 200 days, from April 6 to October 22, 2014. In the dataset, the daily list of donations with the associated donor ID (from which all other information can be extracted) are available. Over these days, about 51 whole blood donations were made on average per day with a total of 10,124 donations. The percentages of blood groups and Rhesus factor were as follows: 33.67% for A Rh+, 5.49% for A Rh-, 10.25% for B Rh+, 1.71% for B Rh-, 3.68% for AB Rh+, 0.56% for AB Rh-, 37.60% for O Rh+, and 7.02% for O Rh-. The historical data show that the number of produced units over these 200 days is highly variable among the days, as shown in Fig. 3.

To create the instance for the test, we have simulated the subsets of booked and non-booked donors, as the possibility of reserving a donation in AVIS Milan is quite new and no significant historical information are available. Thus, to generate the portion of booked donors, existing donors in the historical data are randomly assigned to booked or non-booked class. From a discussion with the managers of AVIS Milan, they declared that a good percentage of booked donors should be at least the 80%. Thus, each donor is independently considered to be booked with probability 0.8, and non-booked with probability 0.2.

For the non-booked donors, we assume that they arrive in the same day as in the historical data. For each booked donor, we use the previous donation date and we compute the first available donation day (90 days after the previous donation for men and 180 days for women); then, date of the reservation call is generated by adding a random number of days, uniformly distributed between 0 and 30, to the first available day.

As for the preallocation model, we consider an appropriate parametric setting from the analysis made in Section 6.1; moreover, we analyze the impact of the coefficients λ_d and λ_f for the prioritization policy of the allocation phase.

Indeed, the preallocation model has been solved considering either the configuration OF1+OF3 (including LB1 in the formulation) and the configuration OF2+OF3 (including LB2 in the formulation), to evaluate the two opposite cases in terms of balancing.

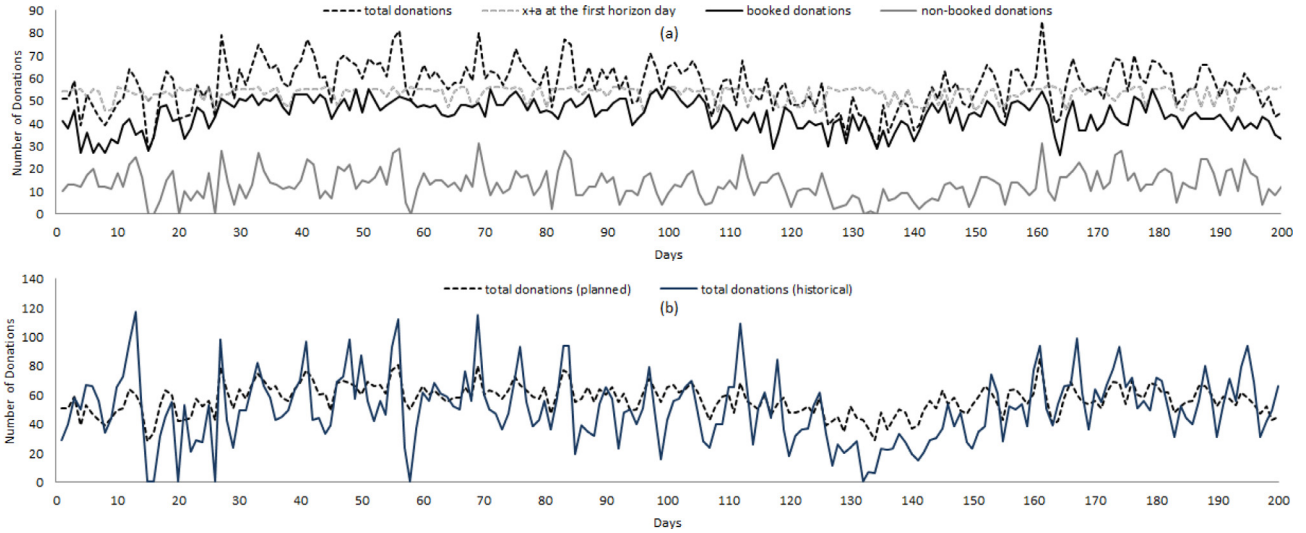


Fig. 8. Number of donations per day for objective function OF1 + OF3, $\varepsilon = 0.25$, and $\lambda_d = 1$ and $\lambda_f = 0$: (a) total number of donations, booked donations, non-booked donations, and $\sum_b x_b^a + a_t^b$; (b) comparison between the total number of donations in the test case and in the observed historical data.

Two levels for the flexibility parameter ε are also considered, i.e., either $\varepsilon = 0$ or $\varepsilon = 0.25$ (the latter to model the observed fluctuations). Moreover, the following parameters have been considered: each day divided in $|K| = 3$ parts; set B made of 8 blood types; $\delta = [0.08 \ 0.06 \ 0.03]$ and $\mu = 0.05$; fractions α_k equal to 0.4, 0.3 and 0.3 for $k = 1, 2, 3$, respectively; capacity c_{tk} equal to 450 minutes $\forall t, k$; all service durations equal to 20 minutes (for both r and R_{tk}). As for a_t^b and R_{tk} , they are daily updated by the rolling approach, starting from no preassignments at the first day. Differently from Section 1 where the time associated with each a_t^b is randomly split among the corresponding R_{tk} , here we exactly track the assigned period k and each preallocated slot directly determines both a_t^b and R_{tk} . Finally, a longer time horizon T equal to 28 days is taken. The remaining parameters are chosen to fit the tested case: the vector of d_b values for the 8 blood types with $|T| = 28$ is assumed as $[503 \ 76 \ 151 \ 22 \ 50 \ 8 \ 602 \ 98]$; the number of non-booked donors n_t^b is assumed to be constant over the days (no trend is observed but just noise) and the vector for the different blood types is set equal to $[3 \ 1 \ 1 \ 0 \ 0 \ 4 \ 1]$. To simulate the real functioning of the BD collection center, the adopted values of parameters d_b and n_t^b have been set to replicate the historical data of the same period (April–October) in previous years (up to 2013). The blood type index b in d_b and n_t^b is intended as follows: $b = 1$ for A Rh+, $b = 2$ for A Rh−, $b = 3$ for B Rh+, $b = 4$ for B Rh−, $b = 5$ for AB Rh+, $b = 6$ for AB Rh−, $b = 7$ for O Rh+, $b = 8$ for O Rh−.

Three different configurations for the prioritization policy are considered. Either we include only the system flexibility (with $\lambda_d = 0$ and $\lambda_f = 1$) or the first available slot policy (with $\lambda_d = 1$ and $\lambda_f = 0$), or we consider both of them together with equal weights ($\lambda_d = 0.5$ and $\lambda_f = 0.5$). The scores S_{tkb} are recomputed after each reservation call is accepted.

A time limit of 1800 seconds and a memory limit of 3 GB have imposed set in each single run of the preallocation model. The lower time limit with respect to the previous analyses has been chosen because of the rolling approach, to fasten the process. Outcomes show that the preallocation model always provides the optimal solution when $\varepsilon = 0.25$, while with $\varepsilon = 0$ the model does not always find the optimal solution in 3 experiments, for a total of 20 out of 600 overall runs. Anyway, even in these cases, the maximum observed optimality gap is 1.18%; thus, we can assess that the considered time limit is enough to derive conclusions.

Results are reported in Figs. 8–13 for the six cases with $\varepsilon = 0.25$, while in the Supplementary Material for the six cases with $\varepsilon = 0$. In all figures, (a) reports, for the 200 rolling days, the number of donations (total number, booked and non-booked) and the $\sum_b x_b^a + a_t^b$ values for the first day of the respective planning horizon (with $t = 1$); (b) reports the comparison between the total number of donations in the test case and in the historical data. Moreover, the waiting times between the reservation call and the donation are reported in Table 6.

Figures show that the approach is able to balance the production of blood units among days. The part related to the booked donations, which can be optimized, is highly balanced in all of the tests. On the contrary, the part related to non-booked donations obviously fluctuates as in the historical data. Globally, comparing the outcomes with the historical data, daily fluctuations are reduced even despite the remaining 20% of uncontrolled non-booked donor arrivals. We remark that the 80% of booked donors was considered because this represents the first goal of AVIS Milan while introducing the reservation system. However, our results show that, despite the good behavior of the approach, a remaining detriment of the balancing is present due to the 20% of non-booked donors. Thus, our suggestion is to implement all promotion policies to bring the highest number of donors to reserve the donation in advance. We also remark that some zeros are present in the historical data, related to holiday days (e.g., Christmas, Easter) that are not considered in our experiments. Anyway, also neglecting these days, we can confirm the reduced fluctuations in our results.

Results presented above refer to all blood types together. However, a similar balancing is obtained while considering each blood type singularly. For instance, we report in Fig. 14 the number of booked donations and the total number of donations, divided by blood type, for the case OF1 + OF3 with $\lambda_d = 1$ and $\lambda_f = 0$. Even though the variability among days is slightly higher than in the total amount of donations, the balancing is mainly guaranteed.

With the first available slot policy, the preallocation model is able to serve most of the donors within the first week, while with the system flexibility policy they are shifted towards the end of the planning period (as shown in Table 6). Moreover, it can be observed that decreasing ε slightly decreases the waiting times of donors. Thus, keeping the flexibility of the system without prioritizing the first available slot is not very effective, with signifi-

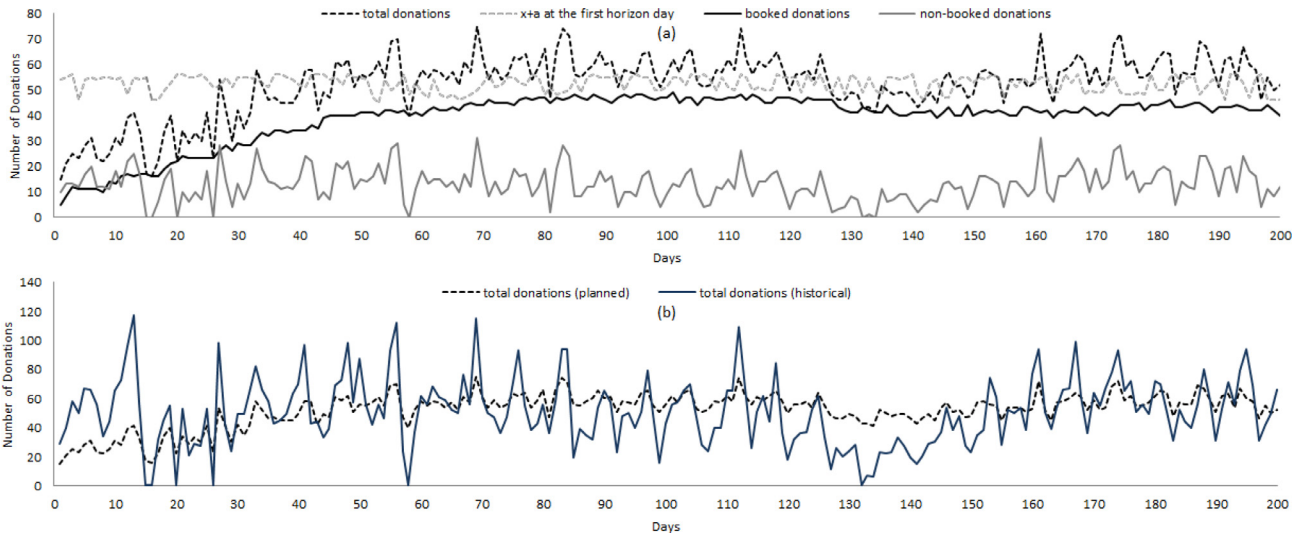


Fig. 9. Number of donations per day for objective function $OF1 + OF3$, $\varepsilon = 0.25$, and $\lambda_d = 0$ and $\lambda_f = 1$. Reported data are as in Fig. 8.

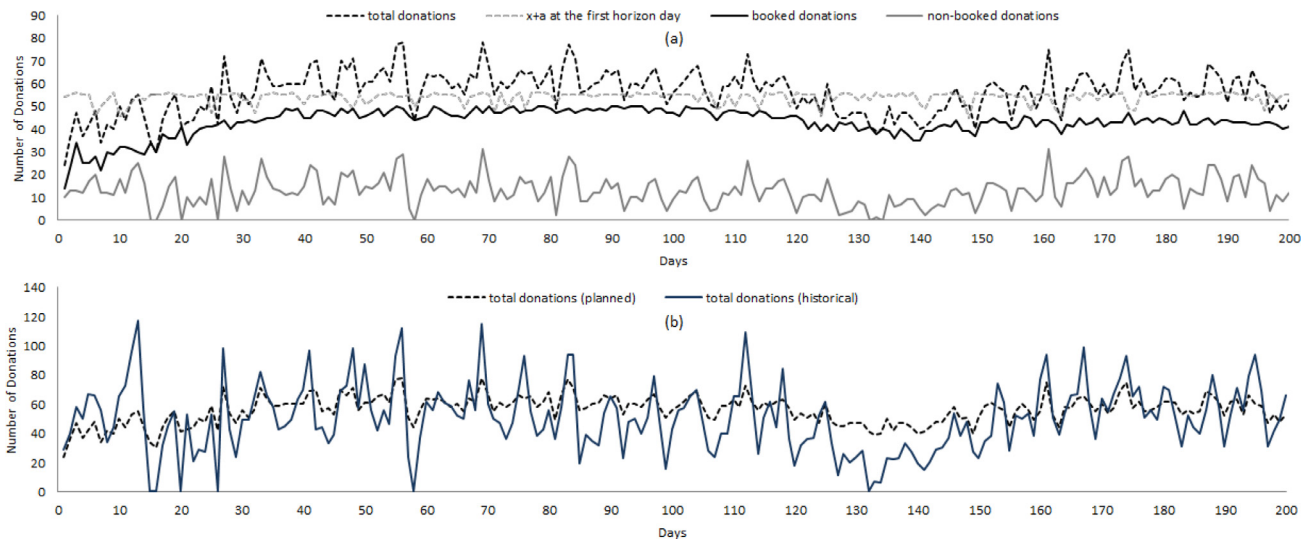


Fig. 10. Number of donations per day for objective function $OF1 + OF3$, $\varepsilon = 0.25$, and $\lambda_d = 0.5$ and $\lambda_f = 0.5$. Reported data are as in Fig. 8.

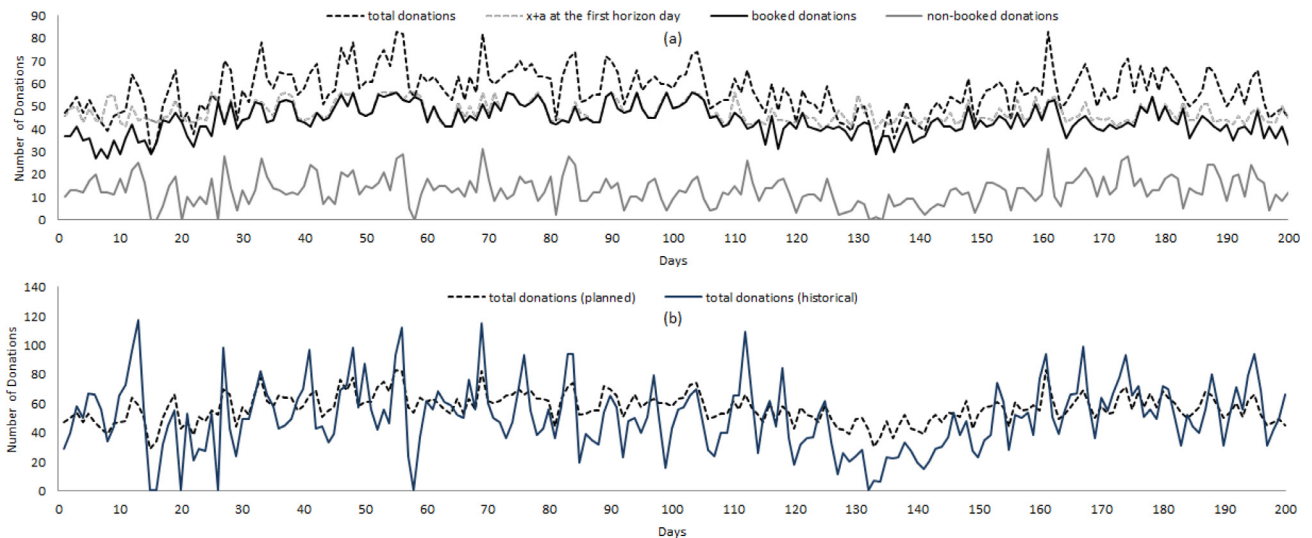


Fig. 11. Number of donations per day for objective function $OF2 + OF3$, $\varepsilon = 0.25$, and $\lambda_d = 1$ and $\lambda_f = 0$. Reported data are as in Fig. 8.

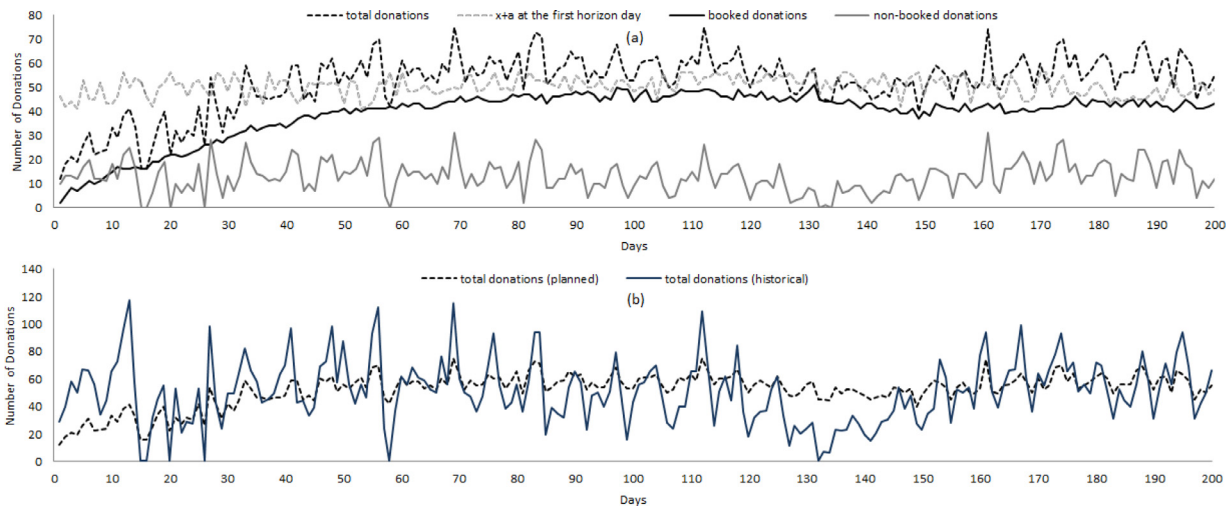


Fig. 12. Number of donations per day for objective function OF2 + OF3, $\varepsilon = 0.25$, and $\lambda_d = 0$ and $\lambda_f = 1$. Reported data are as in Fig. 8.

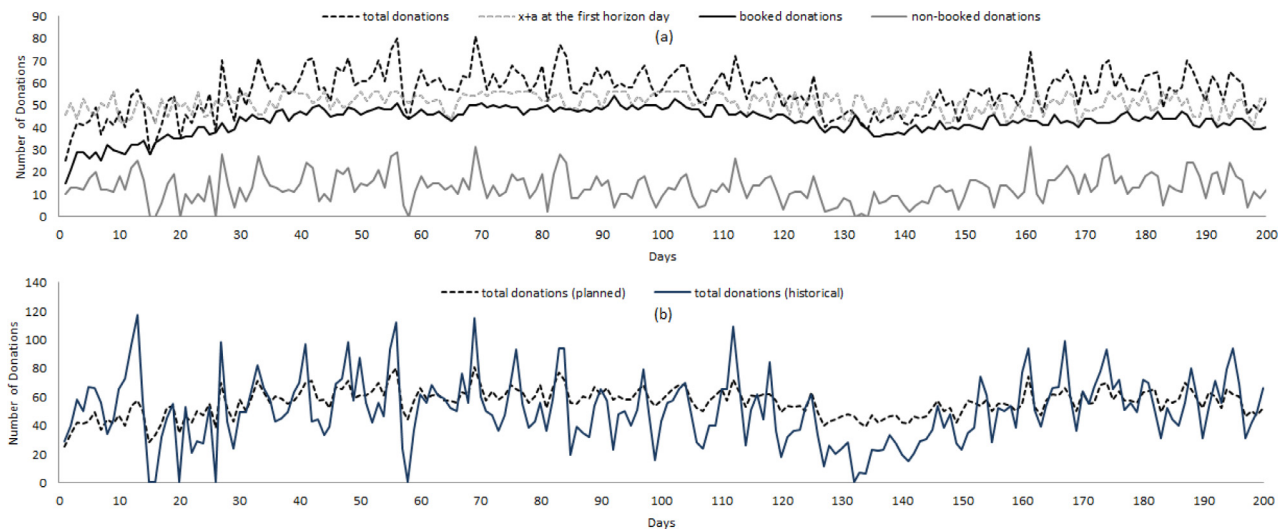


Fig. 13. Number of donations per day for objective function OF2 + OF3, $\varepsilon = 0.25$, and $\lambda_d = 0.5$ and $\lambda_f = 0.5$. Reported data are as in Fig. 8.

Table 6

Waiting time in days between reservation call and donation for booked donors: average and distribution in the last 160 days (excluding the initial ramp-up period of 40 days).

Case	Average	Waiting days distribution			
		0-7 (%)	8-14 (%)	15-21 (%)	≥ 22 (%)
OF1 + OF3, $\varepsilon = 0.25$, $\lambda_d = 1$ and $\lambda_f = 0$	0.48	98.94	0.99	0.05	0.02
OF1 + OF3, $\varepsilon = 0.25$, $\lambda_d = 0$ and $\lambda_f = 1$	22.49	10.15	6.42	6.92	76.50
OF2 + OF3, $\varepsilon = 0.25$, $\lambda_d = 1$ and $\lambda_f = 0$	1.02	98.31	1.61	0.08	0.00
OF2 + OF3, $\varepsilon = 0.25$, $\lambda_d = 0$ and $\lambda_f = 1$	22.60	8.63	6.00	9.42	75.94
OF1 + OF3, $\varepsilon = 0.25$, $\lambda_d = 0.5$ and $\lambda_f = 0.5$	4.93	72.36	26.73	0.91	0.00
OF2 + OF3, $\varepsilon = 0.25$, $\lambda_d = 0.5$ and $\lambda_f = 0.5$	5.27	70.17	27.85	1.98	0.00
OF1 + OF3, $\varepsilon = 0$, $\lambda_d = 1$ and $\lambda_f = 0$	0.30	99.83	0.17	0.00	0.00
OF1 + OF3, $\varepsilon = 0$, $\lambda_d = 0$ and $\lambda_f = 1$	22.27	10.25	6.42	8.04	75.28
OF2 + OF3, $\varepsilon = 0$, $\lambda_d = 1$ and $\lambda_f = 0$	0.33	99.78	0.22	0.00	0.00
OF2 + OF3, $\varepsilon = 0$, $\lambda_d = 0$ and $\lambda_f = 1$	22.42	9.65	5.89	8.84	75.61
OF1 + OF3, $\varepsilon = 0$, $\lambda_d = 0.5$ and $\lambda_f = 0.5$	4.52	75.51	24.08	0.41	0.00
OF2 + OF3, $\varepsilon = 0$, $\lambda_d = 0.5$ and $\lambda_f = 0.5$	4.46	76.81	22.84	0.35	0.00

cantly longer waiting times between reservation call and donation. This has a negative impact on the amount of donations, as longer waiting times reduce the donation frequency. Moreover, without weighting the first available slot, the closest slots might remain empty, thus reducing the daily throughput of the system.

It is worth remarking that, in our tests, we assume that donors always accept the first suggested slot (with the highest score S_{tkb}) without evaluating donors' preferences, who might also ask to donate in a day without any empty preallocated slots. This evaluation requires data that are not included in the AVIS Milan database.

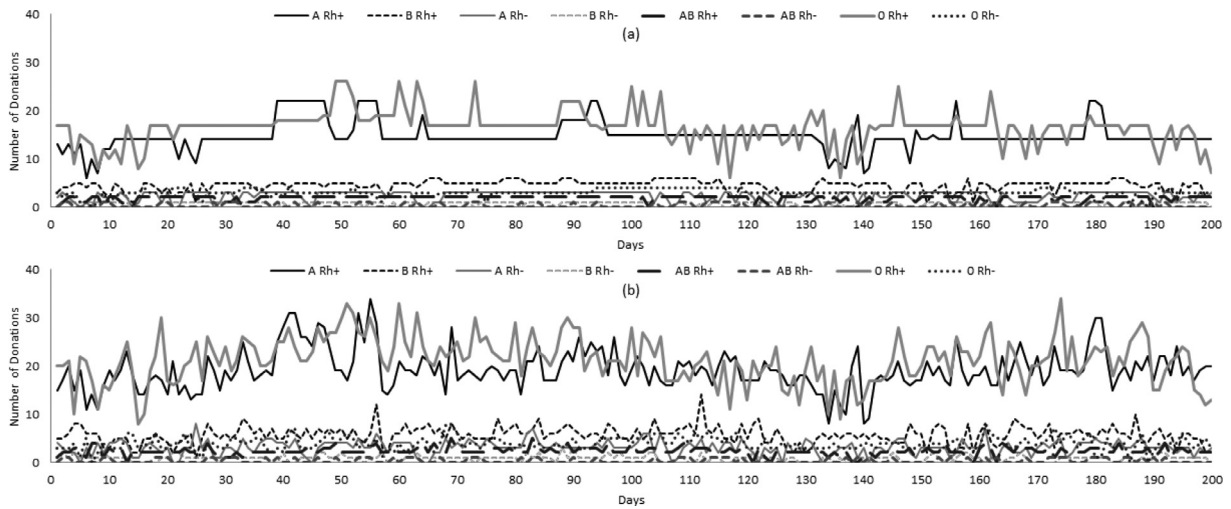


Fig. 14. Number of donations per day, divided by blood type, for objective function OF1 + OF3 with $\lambda_d = 1$ and $\lambda_f = 0$: (a) booked donations and (b) total number of donations. Labels of blood types are reported in increasing order of the associated index b .

Table 7

Mean daily number of booking and non-booking donors (for the Poisson distribution) and d_b vector for the 8 blood types in Groups C.1 and C.2.

Instance		A Rh+	A Rh-	B Rh+	B Rh-	AB Rh+	AB Rh-	O Rh+	O Rh-	Total
C.1	Mean daily booking	15	3	1	1	3	1	18	3	45
C.1	Mean daily non-booking	4	1	0	0	1	0	5	1	12
C.1.1	d_b	418	70	43	20	82	29	461	75	1198
C.1.2	d_b	451	90	28	32	83	20	492	77	1273
C.1.3	d_b	433	74	28	40	85	24	511	98	1293
C.1.4	d_b	413	82	24	33	69	28	526	85	1260
C.2	Mean daily booking	13	3	3	1	1	1	15	3	40
C.2	Mean daily non-booking	3	1	1	0	0	0	4	1	10
C.2.1	d_b	340	75	83	29	28	23	429	73	1080
C.2.2	d_b	365	83	75	33	22	29	464	83	1154
C.2.3	d_b	403	73	102	21	28	29	445	90	1191
C.2.4	d_b	366	85	97	33	24	17	469	97	1188

The two weights λ_d and λ_f also affect the ramp-up period. The number of booked donations are not stabilized until about the 40th day for the cases with $\lambda_d = 0$ and $\lambda_f = 1$. As mentioned, flexibility spreads the donation days over the time horizon, thus letting some slots empty, while on the contrary assigning slots based only on the first available day fills the slots from early beginning, thus avoiding empty slots in the first days when the system starts with $a_t^b = 0$.

In all cases, after the ramp-up period, $\sum_b x_1^b + a_1^b$ at the first day of the planning horizon is really close to the number of booked donations (equal or slightly higher). This indicates both that the d_b parameters have been appropriately set and that, once a fair prediction of d_b is considered, our system does not leave many empty preallocated slots. A slightly higher number of empty slots is present with OF1 + OF3, but this amount is anyway limited.

6.3. Entire approach (randomly generated instances)

We also test the effectiveness of the entire approach on randomly generated instances. We consider a subset of the configurations tested in Section 6.2, to show the effectiveness of the entire approach on other cases through the random generation of scenarios. Indeed, both OF1 + OF3 and OF2 + OF3 alternatives are considered, with only $\varepsilon = 0.25$ and one configuration for the prioritization policy (equal weights $\lambda_d = 0.5$ and $\lambda_f = 0.5$). All other parameters (e.g., $|T|$, $|K|$, δ_k) are set at the same value than in the previous section.

The data generation mechanism is as follows. The number of booking donors who call at each day and the number of non-booking donors who arrive at each day are randomly generated for each blood type according to a Poisson distribution. Different mean values are considered for each blood type and booking/non-booking alternative, while the mean values of the Poisson distributions are the same for each day. Alternative values are considered to generate different layouts. In all cases, the common proportion among the blood types all around the world is respected, being the mean amount of donors belonging to groups A Rh+ and O Rh+ about the 70–80% of the total amount. Moreover, we assume that booked donors are about the 80% of the total, while non-booked ones the remaining 20%. Given a realization of booked and non-booked donors, d_b values are generated with another random process. Indeed, for each blood type b , the sum of the generated booked donors over the rolling days (200 days) is scaled by the ratio between the time horizon T (28 days) and the rolling days. The scaled value is assumed as the mean value of another Poisson distribution, and the value of d_b is drawn from this distribution.

Two groups of instances are defined with this mechanism (as shown in Table 7) and 4 random generations are extracted, each one is characterized by specific d_b values.

The number of donations per day for all of the 8 instances are reported in the Supplementary material. These figures show that also in this case the proposed approach is able to balance blood production over the 200 days. Indeed, compared to the outcomes of the AVIS Milan case (previous section), we even observe slightly

Table 8

Average, minimum and maximum values of booked donors (overall over the blood types) in the last 160 days (excluding the initial ramp-up period of 40 days) for Groups C.1 and C.2.

Instance	Objective function	Average	Minimum	Maximum
C.1.1	OF1 + OF3	45.03	40	50
C.1.1	OF2 + OF3	45.20	38	51
C.1.2	OF1 + OF3	45.96	40	51
C.1.2	OF2 + OF3	46.09	40	51
C.1.3	OF1 + OF3	45.05	40	50
C.1.3	OF2 + OF3	45.24	39	50
C.1.4	OF1 + OF3	45.44	40	51
C.1.4	OF2 + OF3	45.23	39	51
C.2.1	OF1 + OF3	39.23	35	43
C.2.1	OF2 + OF3	39.16	34	44
C.2.2	OF1 + OF3	38.48	33	42
C.2.2	OF2 + OF3	38.91	33	44
C.2.3	OF1 + OF3	39.11	33	43
C.2.3	OF2 + OF3	39.04	32	44
C.2.4	OF1 + OF3	39.53	34	43
C.2.4	OF2 + OF3	39.64	33	44

lower deviations for the total number of donations. In both cases, production unbalancing remains due to the uncontrolled arrivals of non-booked donors.

To briefly compare the 8 instances, we show in Table 8 the number of booked donors for each instance in terms of average, minimum and maximum values. Results shows that in all cases the approach is able to allocate slots according to the mean number of booked donors, which is 45 or for Group C.1 and 40 for Group C.2, respectively (Table 7). Moreover, the small minimum to maximum ranges confirm once again the effectiveness of the proposed approach on production balancing.

As for the waiting times, we observe slightly higher values with respect to the AVIS Milan case. Even though the system is able to serve most of the donors within 14 days as in the AVIS Milan case, here we observe that the ratio of donors served in the first week decreases and donors are shifted to the second week (see table in the Supplementary material).

7. Discussions and conclusion

In this paper, we first define (to the best of our knowledge) and formalize the BDAS problem, and we propose an appointment scheduling framework to solve it.

Our framework for planning the assignments consists of two phases: an MILP model to preallocate time slots of the different blood types, and a prioritization policy to assign the preallocated slots. The goal is to balance the production of blood units of each type among the days, while also avoiding dispersion penalties associated with overtime and donor waiting times. The main points of our framework are, besides the decomposition in two phases, the presence of both booked and non-booked donors and the degree of freedom for the number of slots to preallocate (due to the flexibility associated with d_b). The latter point makes our preallocation model different from the allocation and scheduling models usually available in the literature, since here the amount of entities to allocate is another decision variable, whereas it is fixed in several other cases.

The proposed approach has been successfully applied to the real case of a large blood collection center operating in Italy, the AVIS Milan, and the results confirm the capability of the approach to balance the production of each blood type among days.

Future work will be conducted to extend the model, e.g., to include donations different than the whole blood and to consider missed donations. The latter refers to donors who reserve a donation slot but do not make the donation, because of no-show or

because the physician does not admit them to donation after the visit.

Moreover, to improve the quality of the solution, we will investigate the possibility of creating a robust counterpart of the pre-allocation model. At present, d_b variation is modeled through the flexibility parameter ε , but the model is deterministic. On the contrary, a robust version would include uncertain parameters, at least for d_b and n_t^b .

Finally, further extensions of the preallocation model will be considered to follow an unsteady request for storage, or to integrate the production with the storage management.

Acknowledgments

Authors thank the staff of AVIS Milan for their precious collaboration, and in particular the General Director Dr. Sergio Casartelli.

Supplementary material

Supplementary material associated with this article can be found, in the online version, at 10.1016/j.ejor.2017.08.054.

References

- Alfonso, E., Augusto, V., & Xie, X. (2015a). Mathematical programming models for annual and weekly bloodmobile collection planning. *IEEE Transactions on Automation Science and Engineering*, 12(1), 96–105.
- Alfonso, E., Xie, X., & Augusto, V. (2015b). A simulation-optimization approach for capacity planning and appointment scheduling of blood donors based on mathematical programming representation of event dynamics. In *Proceedings of the 2015 IEEE International Conference on Automation Science and Engineering (CASE 2015)* (pp. 728–733).
- Alfonso, E., Xie, X., Augusto, V., & Garraud, O. (2012). Modeling and simulation of blood collection systems. *Health Care Management Science*, 15(1), 63–78.
- Alfonso, E., Xie, X., Augusto, V., & Garraud, O. (2013). Modelling and simulation of blood collection systems: Improvement of human resources allocation for better cost-effectiveness and reduction of candidate donor abandonment. *Vox Sanguinis*, 104(3), 225–233.
- Ayvaz, N., & Huh, W. T. (2010). Allocation of hospital capacity to multiple types of patients. *Journal of Revenue & Pricing Management*, 9(5), 386–398.
- Baş, S., Carello, G., Lanzarone, E., Ocak, Z., & Yalçındağ, S. (2016). Management of blood donation system: Literature review and research perspectives. In *Proceedings of the 2016 health care systems engineering for scientists and practitioners (HCSE)*. In *Springer Proceedings in Mathematics & Statistics: Vol. 169* (pp. 121–132). Springer.
- Bai, R., Burke, E. K., Kendall, G., Li, J., & McCollum, B. (2010). A hybrid evolutionary approach to the nurse rostering problem. *IEEE Transactions on Evolutionary Computation*, 14(4), 580–590.
- Beliën, J., & Demeulemeester, E. (2008). A branch-and-price approach for integrating nurse and surgery scheduling. *European Journal of Operational Research*, 189(3), 652–668.
- Beliën, J., & Forcé, H. (2012). Supply chain management of blood products: a literature review. *European Journal of Operational Research*, 217(1), 1–16.
- Berg, B., & Denton, B. T. (2012). Appointment planning and scheduling in outpatient procedure centers. In *Handbook of healthcare system scheduling* (pp. 131–154). US: Springer.
- Boonyanusith, W., & Jittamai, P. (2012). Blood donor classification using neural network and decision tree techniques. In *Proceedings of the World Congress on Engineering and Computer Science: Vol. 1* (pp. 499–503).
- Borkent-Raven, B. A., Janssen, M. P., & Van Der Poel, C. L. (2010). Demographic changes and predicting blood supply and demand in the netherlands. *Transfusion*, 50(11), 2455–2460.
- Burke, E. K., De Causmaecker, P., Berghe, G. V., & Van Landeghem, H. (2004). The state of the art of nurse rostering. *Journal of Scheduling*, 7(6), 441–499.
- Cardoen, B. (2010). Operating room planning and scheduling: solving a surgical case sequencing problem. *4OR*, 8(1), 101–104.
- Şahinyazan, F. G., Kara, B. Y., & Taner, M. R. (2015). Selective vehicle routing for a mobile blood donation system. *European Journal of Operational Research*, 245(1), 22–34.
- Do Carmo, B. B., Gurgel, J. L. M., Carmo, B. B. T., Freires Saraiva Jr, A., & de Sena, D. C. (2013). Demand forecast and inventory management: sizing inventory of blood products in a blood bank in brazil. In *Proceedings of the twenty-fourth annual POMs conference*.
- Elalouf, A., Hovav, S., Tsadikovitch, D., & Yedidsion, L. (2015). Minimizing operational costs by restructuring the blood sample collection chain. *Operations Research for Health Care*, 7, 81–93.
- Ferguson, E., & Bibby, P. A. (2002). Predicting future blood donor returns: Past behavior, intentions, and observer effects. *Health Psychology*, 21(5), 513.
- Flegel, W. A., Besenfelder, W., & Wagner, F. F. (2000). Predicting a donor's likelihood of donating within a preselected time interval. *Transfusion Medicine*, 10(3), 181–192.

- Fortsch, S. M., & Khapalova, E. A. (2016). Reducing uncertainty in demand for blood. *Operations Research for Health Care*, 9, 16–28.
- Framinan, J. M., & Ruiz, R. (2010). Architecture of manufacturing scheduling systems: literature review and an integrated proposal. *European Journal of Operational Research*, 205(2), 237–246.
- Gerchak, Y., Gupta, D., & Henig, M. (1996). Reservation planning for elective surgery under uncertain demand for emergency surgery. *Management Science*, 42(3), 321–334.
- Gupta, D., & Denton, B. (2008). Appointment scheduling in health care: Challenges and opportunities. *IIE Transactions*, 40(9), 800–819.
- Gupta, D., & Wang, W. Y. (2012). Patient appointments in ambulatory care. In *Handbook of healthcare system scheduling* (pp. 65–104). US: Springer.
- Gupta, S., & Starr, M. (2014). *Production and operations management systems*. CRC Press.
- Hall, R. (2012). Bed assignment and bed management. In *Handbook of healthcare system scheduling* (pp. 177–200). US: Springer.
- Han, B., Zhang, W., Lu, X., & Lin, Y. (2015). On-line supply chain scheduling for single-machine and parallel-machine configurations with a single customer: Minimizing the makespan and delivery cost. *European Journal of Operational Research*, 244(3), 704–714.
- Hans, E. W., & Vanberkel, P. T. (2012). Operating theatre planning and scheduling. In *Handbook of healthcare system scheduling* (pp. 105–130). US: Springer.
- Jonsson, P., & Ivert, L. K. (2015). Improving performance with sophisticated master production scheduling. *International Journal of Production Economics*, 168, 118–130.
- Klassen, K. J., & Rohleder, T. R. (2003). Outpatient appointment scheduling with urgent clients in a dynamic, multi-period environment. *International Journal of Service Industry Management*, 15(2), 167–186.
- Lim, G. J., Mobasher, A., Kardar, L., & Cote, M. J. (2012). Nurse scheduling. In *Handbook of healthcare system scheduling* (pp. 31–64). US: Springer.
- Liu, N. (2009). *Appointment scheduling in health care*. NC, USA: University of North Carolina at Chapel Hill. Doctoral thesis
- Liu, N. (2016). Optimal choice for appointment scheduling window under patient no-show behavior. *Production and Operations Management*, 25(1), 128–142.
- Liu, N., & Ziya, S. (2014). Panel size and overbooking decisions for appointment-based services under patient no-shows. *Production and Operations Management*, 23(12), 2209–2223.
- Michaels, J. D., Brennan, J. E., Golden, B. L., & Fu, M. C. (1993). A simulation study of donor scheduling systems for the American Red Cross. *Computers & Operations Research*, 20(2), 199–213.
- Mobasher, A., Ekici, A., & Özener, O. O. (2015). Coordinating collection and appointment scheduling operations at the blood donation sites. *Computers & Industrial Engineering*, 87, 260–266.
- Osorio, A. F., Brailsford, S. C., & Smith, H. K. (2015). A structured review of quantitative models in the blood supply chain: a taxonomic framework for decision-making. *International Journal of Production Research*, 53(24), 7191–7212.
- Osorio, A. F., Brailsford, S. C., Smith, H. K., Forero-Matiz, S. P., & Camacho-Rodríguez, B. A. (2016). Simulation-optimization model for production planning in the blood supply chain. *Health Care Management Science*. doi:10.1007/s10729-016-9370-6.
- Oyetunji, E. (2009). Some common performance measures in scheduling problems: review article. *Research Journal of Applied Sciences, Engineering and Technology*, 1(2), 6–9.
- Pierskalla, W. (2005). Supply chain management of blood banks, Springer international series in operations research & management science: Vol. 70. *Operations research and health care* (pp. 103–145).
- Pinedo, M. (2009). *Planning and scheduling in manufacturing and services*. Springer.
- Pinedo, M. (2012). *Scheduling: theory, algorithms, and systems*. Springer.
- Puranam, K., Novak, D. C., Lucas, M. T., & Fung, M. (2017). Managing blood inventory with multiple independent sources of supply. *European Journal of Operational Research*, 259(1), 500–511.
- Rahman, H. F., Sarker, R., & Essam, D. (2015). A real-time order acceptance and scheduling approach for permutation flow shop problems. *European Journal of Operational Research*, 247 (2), 488–503.
- Ritika, A. P. (2014). Prediction of blood donors population using data mining classification technique. *International Journal of Advanced Research in Computer Science and Software Engineering*, 4(6), 634–638.
- Robinson, L. W., & Chen, R. R. (2010). A comparison of traditional and open-access policies for appointment scheduling. *Manufacturing & Service Operations Management*, 12(2), 330–346.
- Samorani, M., & LaGanga, L. R. (2015). Outpatient appointment scheduling given individual day-dependent no-show predictions. *European Journal of Operational Research*, 240(1), 245–257.
- Sawik, T. (2011). *Scheduling in supply chains using mixed integer programming*. John Wiley & Sons.
- Sundaram, S., & Santhanam, T. (2011). A comparison of blood donor classification data mining models. *Journal of Theoretical & Applied Information Technology*, 30 (2), 98–101.
- Testik, M. C., Ozkaya, B. Y., Aksu, S., & Ozcebe, O. I. (2012). Discovering blood arrival patterns using data mining: A method to investigate service quality at blood centers. *Journal of Medical Systems*, 36(2), 579–594.
- Torkki, P. M., Alho, A. I., Peltokorpi, A. V., Torkki, M. I., & Kallio, P. E. (2006). Managing urgent surgery as a process: Case study of a trauma center. *International Journal of Technology Assessment in Health Care*, 22(2), 255–260.
- Truong, V. (2015). Optimal advance scheduling. *Management Science*, 61(7), 1584–1597.
- Van Brummelen, S. P. J., De Kort, W. L., & Van Dijk, N. M. (2015). Waiting time computation for blood collection sites. *Operations Research for Health Care*, 7, 70–80.
- Van Dongen, A., Ruiter, R., Abraham, C., & Veldhuizen, I. (2014). Predicting blood donation maintenance: the importance of planning future donations. *Transfusion*, 54(3 Pt 2), 821–827.
- Wang, J., & Fung, R. Y. K. (2015). Dynamic appointment scheduling with patient preferences and choices. *Industrial Management & Data Systems*, 115(4), 700–717.
- Zhou, Y., & Zhao, X. (2010). A two-demand-class inventory system with lost-sales and backorders. *Operations Research Letters*, 38(4), 261–266.
- Zonderland, M. E., Boucherie, R. J., Litvak, N., & Vleggeert-Lankamp, C. L. (2010). Planning and scheduling of semi-urgent surgeries. *Health Care Management Science*, 13(3), 256–267.