Transportation Research Part E 183 (2024) 103438

Contents lists available at ScienceDirect

Transportation Research Part E

journal homepage: www.elsevier.com/locate/tre

Multi-echelon facility location models for the reorganization of the Blood Supply Chain at regional scale

Antonio Diglio[a], Andrea Mancuso[b,*], Adriano Masone[b], Claudio Sterle[b,c]

[a] University Federico II of Naples, Department of Industrial Engineering (DII), Piazzale Tecchio 80, 80125, Naples, Italy
[b] University Federico II of Naples, Department of Electrical Engineering and Information Technology (DIETI), Via Claudio 21, 80125, Naples, Italy
[c] Institute for System Analysis and Computer Science "Antonio Ruberti" (IASI), National Research Council of Italy, Via dei Taurini 19, 00185, Rome, Italy

A R T I C L E   I N F O

Keywords:
Blood supply chain
Facility location
MILP formulation
Scenario based optimization

A B S T R A C T

Blood and blood products are crucial resources requiring effective management strategies and policies due to the potential severe consequences that could arise from their lack. Over the past two decades, the global healthcare community has recognized the significance of managing the Blood Supply Chain (BSC) efficiently and effectively. This includes policy-making, system design and organization. In this context, the Italian Healthcare Ministry issued a decree aimed at improving the BSC efficiency at regional level while reducing costs by providing several indications and restrictions to be accounted for. To address the need for improved BSC system management and design, we propose a mathematical modeling framework that builds upon and extends multi-echelon facility location and scenario-based mathematical models coming from literature, integrating soft constraints to achieve system aims with a multi-objective viewpoint. The proposed modeling framework has been implemented in two different perspectives: case-based and scenario-based. These two perspectives approaches are conceived to provide a comprehensive solution to the issue at hand, performing sensitivity analysis, and enabling the design of an efficient and effective BSC at the regional level, capable of handling inherent system uncertainty. To this aim, the proposed modeling framework comprises several objectives, including minimizing transportation costs, rationalizing the number and type of facilities, ensuring self-sufficiency, guaranteeing an average accessibility threshold, satisfying imposed restrictions and system constraints, and designing a system robust to varying exogenous and endogenous conditions. Real-world data sets were utilized to test and validate the proposed formulations. The obtained results demonstrate that they can be a valuable decision support tool for decision-makers, providing managerial insights and enabling the simulation of different system configurations.

1. Introduction

Ensuring rapid and safe access to sufficient supplies of blood, as well as safe transfusion processes, is a fundamental component of any strong healthcare system worldwide (World Health Organization et al., 2017). Blood transfusions play a vital role in disaster situations, accidents, trauma cases, emergencies, and in aiding women suffering from bleeding related to pregcy and childbirth.

* Corresponding author.
E-mail addresses: antonio.diglio@unina.it (A. Diglio), andrea.mancuso@unina.it (A. Mancuso), adriano.masone@unina.it (A. Masone), claudio.sterle@unina.it (C. Sterle).

https://doi.org/10.1016/j.tre.2024.103438
Received 5 September 2022; Received in revised form 18 January 2024; Accepted 25 January 2024
Available online 20 February 2024
1366-5545/

In countries with sufficiently developed healthcare systems, blood and blood products also provide critical support for medical procedures like transplantation and major surgeries. In addition, they help treat immune deficiency conditions and diseases related to blood and bone marrow (World Health Organization et al., 2017).

Human blood is considered a scarce resource, and wasting it is unacceptable, as it can lead to postponed surgeries, untreated patients, or even death (World Health Organization, 2021). However, in many developing nations, the unavailability of safe blood contributes to a high number of deaths, even in some urban healthcare facilities. Voluntary donation remains the only source of blood; however, it has some drawbacks, including limited donor numbers, delays in testing, and a high risk of product perishability (Pirabán et al., 2019). While artificial blood or blood components could serve as alternatives, they are not currently feasible options and remain an area for future research and development.

In this context, effective Blood Supply Chain (BSC) management is a crucial issue for developed and developing countries. The BSC involves six processes related to blood, namely: collection, testing, blood processing, storage, distribution, and transfusion. These interrelated activities require coordination among five key players: donors, mobile collection sites (CSs), blood centers (BCs), demand points (such as hospitals or transfusion points), and patients (Pirabán et al., 2019). Thus, managing the BSC can be a daunting task due to the complexity of the processes and the need for precise coordination among the various players involved. Nonetheless, it is crucial to ensure a safe and sufficient supply of blood and blood products for transfusions, as this measure plays a vital role in saving lives and enhancing health outcomes.

Therefore, optimal decision-making in BSC management is necessary to minimize shortages and waste, as well as to design a more efficient, effective, and robust system. Accordingly, as we discuss in the next section, the literature flourishes with contributions that, despite the shared problem setting, mainly differ for the specific application context and peculiarities of the national/regional case study.

This study focuses on the Italian BSC, which has been the subject of ongoing efficiency-oriented reforms and suffers from a relatively high fragility concerning blood demand satisfaction objectives (i.e., the so-called *self-sufficiency* goal).

In Italy, the management of the BSC falls under the responsibility of the Transfusion System, a public body that is part of the Italian National Health Service (NHS) established in 1978. The Italian BSC relies entirely on voluntary and unpaid donations, as in many other countries. In 2020, there were 2,893,788 donations, comprising 2,438,349 whole blood donations and 455,439 apheresis donations. These donations were contributed by 1,626,506 donors, including 1,352,162 periodic donors and over 355,174 occasional first-time donors, resulting in 2,822,504 transfusions (Catalano et al., 2021). However, the system is vulnerable and lacks robustness when faced with fluctuations in blood demand, as evidenced by the minimal difference of only 71,284 units (2.5%) between donations and transfusions. In other words, an increase in blood demand (or, to the contrary, a decrease in donations) may easily yield severe difficulties in meeting the required yearly number of transfusions, thus risking the system's self-sufficiency.

In addition, in 2013, the Italian government published a national guideline for regional authorities related to blood and its components in compliance with the European Directive 2002/98/EC (Gazzetta Ufficiale, 2013). The guideline introduced efficiency measures that require collection processing activities, such as blood analysis, separation of blood components, and transformation into plasma-derived products, to be consolidated in fewer BCs. According to the recommendation, each BC should process a minimum of 40,000 units per year. However, this target is significantly higher than the average productivity of BCs in all Italian regions. Indeed, there are 278 BCs spread across the country, and considering the aforementioned 2,893,788 donations (Ministero della Salute, 2021), this results in an average productivity of 10,409 units per BC. Therefore, the ongoing reorganization of the Italian regional BSC emphasizes the importance of providing stakeholders with a tool to rationalize and enhance its functioning, while ensuring an adequate supply of blood and blood products.

In this context, this work focuses on the first leg of the Italian BSC, i.e., the blood collection, which is the BSC activity mostly impacted by previously discussed reforms.

The regional authorities have identified two main strategic actions to enhance BC productivity. The first action involves reducing the number of employable BCs by selecting those to be shut among the existing ones. The second consists of resorting to Mobile Units (MUs) to reach isolated blood donation points and increase processing levels at each BC. In addition, as proposed in Bruno et al. (2019) and Diglio et al. (2021), we also consider the possibility of downgrading existing BCs to the so-called Blood Stations (BS), where only collection activities are carried out. Subsequently, the blood collected at the BSs is dispatched to the BCs for processing. Since the distance to travel in order to reach the collection facility deeply influences the aptitude to donate blood, the introduction of BSs should mitigate the distance negative effect on donors' donation propensity. In the following, when no distinction is needed, we refer to both BCs and BSs as Blood Facilities (BFs).

On this basis, in a nutshell, in line with the previous literature on the topic presented in Bruno et al. (2019) and Diglio et al. (2021), the main contribution of this work comprises the proposal of a mathematical modeling framework that can serve as a decision support tool for the strategic redesign of an existing regional BSC. More precisely, the proposed framework rationalizes the BSC collection structure by closing unnecessary BCs, downgrading BCs to BSs, and supporting collection processes through Mobile Units (MUs). Such facilities, together with donors, configure a multi-echelon network system. The overall objective is to minimize the blood transportation cost (from collection to processing facilities). Moreover, specific system tactical requirements are also considered, such as maximum and minimum capacities for collection and processing activities, respectively, as well as the need to satisfy the total regional demand for blood (i.e., the self-sufficiency goal). The latter are formulated as soft constraints, and their violation is accounted for in the objective function by adopting a penalty-based method. This method allows the evaluation of a range of different trade-off solutions between the minimization of BSC transportation costs and compliance with the above requirements. Finally, donors' accessibility is also envisaged. Specifically, we ensure that the average distance potential donors should travel to reach the facilities is below a maximum threshold. Based on this design choice, the rationalization of the existing network is expected to maintain the capillary presence of blood facilities over the territory.

The proposed modeling framework has been implemented in two different perspectives: case-based and scenario-based. The first one is designed to reorganize a BSC in situations characterized by known, steady, and regular donations. Conversely, the second formulation is conceived to address the uncertainty in yearly donations and their potential variations. These two perspectives enable to perform a twofold investigation enriching the understanding of the problem and enhancing the quality of the decision-making process. On the one hand, the case-based formulation allows to perform a sensitivity analysis with respect to the donations' propensity and the system average accessibility, which represent the main factors affecting the strategic decision under investigation. On the other hand, the scenario-based formulation allows to handle inherent system uncertainty issues by designing BSC solutions which are robust with respect to the yearly donation propensity, accounting for expected value and worst-case scenarios. Both formulations, being extensions and modifications of the one presented in Diglio et al. (2021), represent a methodological advancement in the field. In particular, they introduce explicitly the accessibility issue and configure mixed-integer linear programming (MILP) models for multi-echelon facility location problems with soft constraints that allow for considering the system targets in a multi-objective fashion. Moreover, strengthening valid inequalities are also proposed to improve the computational performance when dealing with the solution of large size instances by off-the-shelf optimization software.

The proposed formulations are tested using real data from three Italian regions (i.e., Campania, Apulia, and Lombardy — representing mid-to-large-scale test cases and characterized by different topologies), evaluating two blood collection management strategies, namely:

1. a *centralized strategy* where the entire region is managed as a single unit, as previously shown in Diglio et al. (2021).
2. a *decentralized strategy* where the region is divided into different areas to prevent polarization caused by heavily populated cities, thereby ensuring a more significant presence of BFs throughout the territory for improved average accessibility.

The experimental results demonstrate the capability of the modeling framework in handling real-world instances, thus confirming its usability as a valuable decision-support tool. Indeed, on the one hand, it allows to derive useful managerial insights, and, on the other hand, it enables the simulation of different system configurations, operational conditions, and working scenarios. Notably, we show that all the instances are solved in acceptable computational times through an off-the-shelf solver, which makes it potentially interesting for practitioners seeking support in policy-making.

The rest of the paper is organized as follows. Section 2 provides a comprehensive literature review on facility location approaches for BSC design problems to highlight the application and methodological contribution of this work. In Section 3, we present a formal description of the problem, while the developed mathematical models are given in Section 4. In Section 5, we report on the selected case studies and present an analysis of the results obtained from our experiments. Finally, Section 6 closes the paper with some conclusions and potential avenues for future research.

2. Literature background and positioning of the current contribution

Operations Research is widely recognized as an essential tool for decision support in healthcare planning and management. The use of optimization techniques in healthcare has received significant attention over the past three decades, as evidenced by Rais and Viana (2011) and Ahmadi-Javid et al. (2017). In this research domain, Blood Supply Chain management is an area of growing interest, dealing with a broad spectrum of strategic, tactical, and operational problems. For a comprehensive overview on the topic, the interested reader is addressed to Beliën and Forcé (2012), Osorio et al. (2015), Pirabán et al. (2019), and Meneses et al. (2022). In particular, the latter reference provides an insightful conceptualization of the different typologies of problems relevant to BSC management – classified by planning level – and the main decisions involved.

At the *tactical* and *operational* planning level, typical problems concern the definition of short-to-mid-term optimal collection, production, transportation, and administration policies of blood units and derivatives (and their daily scheduling) occurring at collection/production facilities or demand nodes (i.e., hospitals — see, e.g., Hamdan and Diabat, 2019; Liu et al., 2020; Osorio et al., 2018, to name a few).

At the *strategic* level, instead, the focus is on the long-term (re-)design of BSC networks, which usually calls for the optimal siting of BFs and, eventually, the adequate definition of their sizes/capacities. Therefore, BSC network design problems are often rooted in the *Facility Location* literature (FLPs, see Laporte et al., 2019).

As discussed in Meneses et al. (2022), BSC management problems concerning different planning levels have been rarely treated in a fully-integrated manner. Indeed, the complexity of the interconnections among the system's components and operations may easily lead to intractability. However, it is widely recognized the significant impact of appropriate design strategic decisions on the tactical and operational performance of the whole BSC (Bruno et al., 2019).

In this context, this work mainly focuses on the long-term planning problem related to the design and structure of the BSC under *ordinary conditions*, i.e., not motivated by emergencies and disaster scenarios (see Rameshwar et al., 2019 and the references therein). Thus, it falls within the strategic level problems. Nevertheless, as suggested in Meneses et al. (2022), in order to consider the inter-dependency among the levels, several tactical decision related to collection, productivity and transshipment policies are integrated within the proposed framework. Notably, various scholars investigated such problems by resorting to multi-echelon facility location/allocation models and solution methods. As discussed in Attari et al. (2018), the literature can be classified on the basis of four main criteria: data availability, length of the time horizon, involved processes and structure of the system (in terms of number of echelons and type of facilities and their interactions).

Similar classifications and tabular comparisons are also provided in Pirabán et al. (2019), Hamdan and Diabat (2019) and Momenitabar et al. (2022). On the other side, we observed the lack of classification concerning specific operational constraints of the system. This omission is primarily because most of the literature focuses on real case studies with unique requirements and definitions for blood facility features. Such diversity could result in a potential misclassification when attempting to categorize these issues.

Accordingly, in order to better motivate the proposed case-based and scenario-based formulations, in the following, we provide a concise review of some recent contributions in the field, dividing them in two groups – namely deterministic and uncertainty based – highlighting for each of them the main aspects related to the these criteria.

Concerning deterministic approaches, Cetin and Sarul (2009), consider the problem of determining the optimal location of blood banks and their allocation to hospitals, seeking to minimize the related costs. To this end, a multi-objective, single-period, and deterministic model was developed, which was then tested on small-sized numerical examples. Thus, donors allocation is not explicitly considered

In Şahin et al. (2007), the real problem of regionalizing blood services in Turkey was addressed. The authors considered a hierarchical structure involving higher-level facilities, the so-called Regional Blood Centers, and three lower-level facilities, i.e., BCs, BSs and MUs. The authors tackled the problem by solving a series of subsequent deterministic, single-period mathematical models. In practice, the envisaged location–allocation decisions are not taken in an integrated fashion. Note also that no capacity restrictions were considered, nor the actual distribution of donors was explicitly taken into account.

A slightly different problem was investigated by Elalouf et al. (2015), who devised a mathematical model for the optimal location of centrifuge centers, responsible for blood separation, and the allocation of clinics, in charge of blood collection. The authors sought to maximize the total profit gained by a health management organization operating in Israel. As in Şahin et al. (2007), donors and capacity-related decisions were not involved.

Chaiwuttisak et al. (2016) developed a single-period deterministic model to locate two types of collection facilities and decide their optimal allocation to processing facilities, seeking to optimize transportation costs and the amount of donated/processed blood under a budgetary constraint. The model was tested on the Thai Red Cross case study, using the 76 capitals of Thailand as candidate locations and assuming donated blood at each candidate location as known beforehand (that is, donors and capacities were not explicitly considered).

Finally, in Bruno et al. (2019), the problem of redesigning an existing network of BCs – responsible for collection and processing activities – was tackled, by means of the following decisions: downgrading a BC to a BS, performing only collection, or closing it. The authors devised a deterministic and single-period model, including donors and BSs-to-BCs allocation decisions, aimed at minimizing location and transportation costs. The method was extensively tested on a relatively large-sized case study corresponding to an entire Italian region. For the same problem, some of the same authors introduced several soft constraints to deal with capacity and demand satisfaction requirements – whose corresponding shortages/surplus were penalized in the objective function – and blood units transportation costs in a multi-objective-like fashion (see Diglio et al., 2021).

Concerning instead uncertainty based approaches, Zahiri et al. (2015) studied the problem of locating capacitated fixed and temporary BFs over a multi-period planning horizon, intending to satisfy the total demand for blood in each period at the minimum location and transportation cost. Donors' allocation decisions were also included. Specifically, a covering radius was considered for donors to reach a located facility. To model the problem, a robust possibilistic mathematical program accounting for the uncertain nature of some relevant parameters was proposed, which was tested on a relatively small-sized randomly generated instance. In a follow-up paper (Zahiri and Pishvaee, 2017), the above work was extended by considering blood group compatibility.

A similar problem setting, both in terms of network structure and decisions involved, was explored in Ramezanian and Behboodi (2017), where a robust optimization model motivated by uncertainty on blood demand at hospitals was developed. In the proposed model, inventory and shortage costs at hospitals were also considered. Experiments were run on a small case study from the city of Teheran (similar to that in Jabbarzadeh et al., 2014), characterized by 22 donor groups – corresponding to the 22 city districts – with the latter being also regarded as potential locations for BFs.

A two-stage stochastic programming model was proposed in Attari et al. (2018) where two types of facilities, i.e., Blood Collection Centers and Blood Collection and Processing Centers, had to be located over a discrete multi-period planning horizon. First-stage strategic variables referred to the location of the above-mentioned facilities and appropriate allocation decisions. Second-stage (scenario-dependent) decisions, instead, were related to the shipment of collected blood units based on the first-stage allocation decisions. The East Azerbaijan Province case was used to illustrate the performance of the model and of the developed accelerated Benders' decomposition approach.

In Samani et al. (2019) a robust fuzzy mathematical model for the optimal location of capacitated blood collection facilities in a multi-period setting was developed, with the main novelty of the work being in the multi-attribute group decision-making approach used to account for both qualitative and quantitative factors in the network design problem. The authors performed their empirical tests on the small case of the city of Tabriz in Azerbaijan (ten donors' locations and less than ten potential locations for blood facilities).

In Moslemi and Pasandideh (2021), a multi-period model for the location of blood collection and blood processing facilities under stochastic hospital demands was proposed. The model optimized two objective functions: (i) the total costs and (ii) the total time (e.g., transportation/processing) in the BSC. Note that donors were not explicitly considered, as the number of blood units collected was regarded as an exogenously given parameter. The so-called "Interval Evidential Reasoning" approach was used to handle uncertainty, and evolutionary genetic algorithms were used as solution approaches. Numerical illustrative tests were performed on randomly generated instances.

Arani et al. (2021) focused on the design of a BSC network comprising donors, blood collection facilities, blood centers, and hospitals. Notably, no location decisions were considered. Instead, optimal allocation and inventory policies were explored to simultaneously optimize environmental, social, and economic objectives under uncertainty on both supply (i.e., donations) and demand. Later on, a similar problem setting has been considered at the core of the developments presented in Momenitabar et al. (2022). In particular, the latter reference mainly emphasized sustainability aspects related to the closed-loop nature of the investigated BSC.

Finally, a single-period model for BSC network design under uncertainty on donations, demand, and blood disposal rates was designed in Tirkolaee et al. (2023), with the aim of optimally locating three types of facilities: Blood Donation Centers (BDCs), Blood Centers (BCs), and Regional Hospitals (RHs), seeking to minimize the total costs (location, transhipments, wastage). The investigated BSC also involved donors and final hospitals, although the geographical distribution of donors (and their allocations) was not considered. The authors employed an interactive possibilistic programming approach to solve the problem, tested on the case of Teheran (19 BDCs, two BCs, six RHs, and 23 hospitals).

Looking at the above discussed contributions, our work differentiates with previous literature review in two main perspectives, namely the application field and methodological approach.

Concerning the application perspective, it is easy to note that most of the contributions deal with very specific BSC design problem deriving from the national/regional context under investigation. Thus, also related solution approaches are highly application-dependent, and their usage cannot be straightly replicated and/or extended to other situations. The approach proposed in this work is specifically outlined for the Italian BSC. Nevertheless, since it is motivated by the transposition of a European Directive, contrarily to the previous ones, it could actually represent a baseline to be used and particularized in the reorganization of the BSCs of other European countries. Finally, it is also worth noting that in most of the previous literature, probably for the sake of tractability, the investigated case studies are relatively small in terms of cardinality of the involved sets, thus being only partially representative of real-world problems. Instead, our contribution deal with large scale test cases built upon a real dataset, thus providing an accurate system sketch and simulation of the BSC functioning.

Concerning instead the methodological perspective, consistently with the specific applications under investigation, this work differentiates from previous literature for one or more of the following features characterizing a BSC design problem, i.e.: donor allocation decisions; capacity, productivity and self-sufficiency constraints; number of echelons; functioning mechanism; targets to be optimized.

To the best of the authors' knowledge, no contribution in the literature deals with a multi-echelon BSC system envisaging simultaneously capacity, productivity, self-sufficiency and accessibility constraints, within a unique multi-objective framework in deterministic and uncertain settings. Some similarities can be found just in Bruno et al. (2019) and Diglio et al. (2021), which represent the first and only works specifically dealing with the problem under investigation. Nevertheless, this work provides the following advancements: it provides a modified and integrated MILP deterministic formulation, strengthened by valid inequalities, and envisaging accessibility issue; it extends the deterministic formulation introducing the scenario-based formulation in order to deal with uncertainty on donation propensity; finally, it presents an extensive experimental campaign aimed at simulating different collection strategies and performing both a sensitivity analysis and an evaluation for expected value and worst-case scenarios.

3. Problem description and assumptions

Referring to a generic region in Italy, we consider the existence of a discrete set of pre-existing BFs responsible for blood collection and processing activities. In our terminology, following the literature (see Şahin et al., 2007), we refer to these facilities as BCs. Additionally, we assume the presence of a discrete set of points representing potential locations of blood donors. We posit that the propensity of donors to donate blood is denoted as the "*donation rate*", which remains constant across all points. The donation rate is expressed as the number of donations per 1000 inhabitants, estimated using publicly available data. In addition, given that blood donations are voluntary and unpaid, we reasonably assume that distance plays a crucial role in influencing the propensity to donate. Hence, we postulate that donors are more likely to visit a BC if it is within a maximum distance from their geographical location, referred to as the "*reachability threshold*". The objective of the BSC is to ensure "*self-sufficiency*" within the healthcare system, meaning that the annual demand for blood units transfused at hospitals is adequately met. According to national government guidelines (see Catalano et al., 2021), BCs should achieve a *minimum productivity* level of 40,000 blood units per year to maintain accreditation. However, current data indicates that the actual number of blood units processed per BC falls significantly below this threshold (refer to Ministero della Salute, 2021). Consequently, strategies to enhance the efficiency of regional BSCs are being sought. In this regard, rationalizing the BSC by reducing the number of active BCs presents a viable possibility. However, it is crucial to ensure the widespread presence of BFs across the territory, as it strongly influences donation rates and, therefore, self-sufficiency. Thus, we consider the following potential decisions:

- Keep an existing BC active, holding both collection and processing activities;
- Downgrade a BC into a BS, performing collection activities only;
- Closing a BC and not using it anymore.

Clearly, donors have the option to make donations at both BSs and BCs within the reachability threshold. It is reasonable to assume that they would choose the closest facility (referred to as "*closest assignment*"). Furthermore, as discussed in Section 1, the data indicates that donations predomitly come from periodic and healthy donors. Therefore, in this paper, we make the following

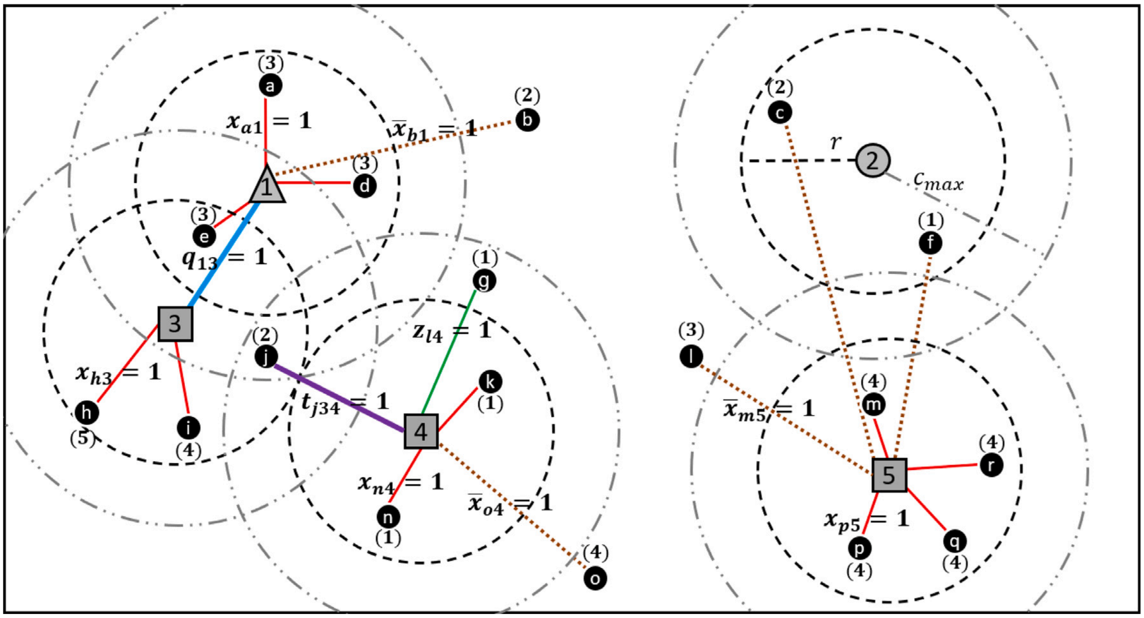


Fig. 1. Illustration of a *BSC-MFLP-CB* solution, related setting and parameters (Note: Black dots — donation points; Gray triangles — BSs; Gray Squares — BCs; Gray Circles: closed BFs; Black dashed line circles: area within the reachability threshold from each BF; Gray dashed line circles: area within the degradation threshold from each BF; Red lines: x-variables; Green lines: z-variables; Blue bold lines: q-variables; Purple bold lines: t-variables; Brown dotted lines: $\bar{x}$-variables).

assumptions:

- donors are defined as the percentage of the population in a given area who make donations, based on the donation rate;
- all donors, within the reachability threshold of a located BS or BC, will perform donations;
- all collected blood units will be processed.

Blood units collected at BSs need to be transferred and processed at an active BC. Since blood is a perishable product that degrades quickly, we assume that such transfers are allowed only between a BS and a BC located within a maximum given distance ("*degradation threshold*"). By adopting this approach, we aim to align the resulting system with regulatory frameworks by consolidating production in a reduced number of BCs. Together with BSs, these facilities ensure a widespread presence of collection points for users. Additionally, to prevent the consolidation of collection activities, we further assume that there is a maximum capacity for blood units at BCs and BSs due to limited personnel availability. Specifically, we assume a maximum capacity for blood collection only at BCs or BSs. This is necessary because medical staff is required to oversee and manage the donation process. In terms of productivity, there is no need to establish a fixed capacity since these activities rely primarily on specialized machinery and equipment, resulting in shorter processing times and uninterrupted operation. Instead, according to the reform, minimum productivity requirements at BCs are considered. To meet them, the allocation of BSs-to-BCs is left a network design choice, i.e., no closest assignment is enforced. Furthermore, we consider the possibility of utilizing MUs to support collection activities. Specifically, we assume the availability of a limited fleet of MUs responsible for collecting blood units from specific donor locations and transporting them to a BC within the degradation threshold. It is important to note the significant implications of using MUs to ensure compliance with policy requirements within the BSC. Firstly, it enables reaching more isolated donor locations for self-sufficiency. Secondly, it helps meet the maximum collection capacity constraint at located BCs and BSs by reducing the number of blood units collected there. Lastly, as the allocation of MUs to BCs is a network design choice, it can enhance minimum productivity levels at BCs. Therefore, as for the BSs-to-BCs allocations, blood collected by MUs does not have to be necessarily transferred to the closest BC. These aspects are further clarified through a toy-example depicted in Fig. 1 and presented in Section 4 to provide a clearer exposition of the introduced mathematical notation. Considering that the envisaged reorganization process involves a reduction in available BFs and recognizing the public utility of the BSC, we additionally assume that the decision-maker is interested in avoiding a significant deterioration in donors' accessibility to the service. To achieve this, we ensure that the average distance between donors and a located BF remains below a maximum threshold value (referred to as "*accessibility threshold*"), thus maintaining the presence of BFs spread across the territory. It is worth noting that overall accessibility considerations encompass all potential donors in the region. Although only a subset of donors is considered for self-sufficiency in our problem setting, even those located farther from a BS or BC than the reachability or degradation thresholds may theoretically donate blood.

In a nutshell, our problem involves a multi-echelon BSC network consisting of donors, MUs, BSs, and BCs. Location and allocation decisions need to be made to fulfill three primary requirements: (i) achieving self-sufficiency, (ii) ensuring maximum capacity collection at BSs, and (iii) maintaining minimum productivity levels at BCs. We assume that the decision-maker is interested in evaluating solutions that strike a balance between minimizing transportation costs for blood units (from BSs and MUs to BCs) and complying with the aforementioned requirements. This aligns with the ongoing process of reorganizing regional BSCs, where fully adhering to these requirements may not be feasible in practical terms due to existing vulnerabilities. To address this, as we will demonstrate, these conditions will be formulated as soft constraints, and any violations will be accounted for in the objective function using a penalty-based approach. In the following, for the sake of readability, the problem will be denoted as BSC-MFLP, i.e., Blood Supply Chain Multi-echelon Facility Location Problem.

4. A mathematical modeling framework for the reorganization of regional BSC

The objective of this paper is to devise a mathematical modeling framework to tackle the BSC-MFLP at regional level in Italy. We recall that our modeling framework envisages two perspectives: case-based and scenario-based. In the following, these are referred to as *BSC-MFLP-CB* and *BSC-MFLP-SB*, respectively. Hereafter, we first describe the notation used to model the *BSC-MFLP-CB* in Section 4.1. The related mathematical formulation is given in Section 4.2. Then, Section 4.3 focuses on the scenario-based case, i.e., the *BSC-MFLP-SB* formulation. Finally, in Section 4.4, we present some model enhancements based on strengthened constraints re-formulations and valid inequalities.

4.1. Notation

To formulate the *BSC-MFLP-CB*, we introduce two primary sets: the set of potential BF locations, denoted by J, and the set of donor locations/points, represented by I, whose generic elements are denoted as i and j, respectively. The population of each location i, $i \in I$ is represented by p_i, and, being α the donation rate, the quantity of collectable blood units at point i is calculated as $a_i = \alpha \cdot p_i$ (expressed in thousands units). The donors-to-facility distances for each pair $(i, j), i \in I, j \in J$ are denoted by d_{ij}, while we use c_{jk} for the mutual distances between facilities $(j, k) \in J$. Besides, let r and c_{max} be the reachability and degradation thresholds, respectively. Finally, let us define a *big M* parameter F, $F = max_{i\in I, j\in J} d_{ij}$.

On this basis, the following sets are defined:

- N_i: set of BF locations j, $j \in J$, such that their distance from the donation point i, $i \in I$, is at most equal to reachability threshold ($d_{ij} \le r$);
- S_j: set of donation points i, $i \in I$, such that their distance from the BF location j, $j \in J$, is at most equal to reachability threshold ($d_{ji} \le r$);
- M_j: set of facilities k, $k \in J$, such that their distance from the BF location j, $j \in J$, is at most equal to the degradation threshold ($c_{jk} \le c_{max}$). Moreover, we define also $M_j^+ = M_j \cup \{j\}$;
- O_i: set of BF locations j, $j \in J$, such that their distance from the donation point i, $i \in I$, is at most equal to the degradation threshold ($c_{ij} \le c_{max}$);
- T_j: set of donation points i, $i \in I$, such that their distance from the BF location j, $j \in J$, is at most equal to the degradation threshold ($d_{ji} \le c_{max}$).

Moreover, the following additional non-negative parameters are introduced: annual regional blood demand (D); blood collection minimum productivity (P_{min}); BF maximum collection capacity (C); number of available Mobile Units (n); penalty factors for productivity shortage (λ_1), capacity overrunning (λ_2), and blood self-sufficiency shortage (λ_3).

Given this setting the following binary decision variables are introduced:

- *Location variables*
  - $y_j^s \in \{0, 1\}$, $j \in J$: each variable assumes value 1 if location j is selected for a BS, 0 otherwise.
  - $y_j^c \in \{0, 1\}$, $j \in J$: each variable assumes value 1 if location j is selected for a BC, 0 otherwise.
- *Assignment variables*
  - $x_{ij} \in \{0, 1\}$, $i \in I$ and $j \in N_i$: each variable assumes value 1 if donation point i is assigned to a BF in j, 0 otherwise.
  - $z_{ij} \in \{0, 1\}$, $i \in I$ and $j \in O_i$: each variable assumes value 1 if donation point i is assigned to an MU which collects the blood and transfers it to a BC in j, 0 otherwise.
- *Blood transfer variables*
  - $q_{jj'} \in \{0, 1\}$, $j \in J$ and $j' \in M_j^+$: each variable assumes value 1 if the blood collected at a BF in j is transferred to a BC in j', 0 otherwise.
  - $t_{ijj'} \in \{0, 1\}$, $i \in I$, $j \in N_i$ and $j' \in O_i$: each variable assumes value 1 when donation point i, who could be assigned to an open BF in j, is served by an MU that collects the blood and transfers it to a BC in j', 0 otherwise.

On this basis, we can infer that, given a BSC solution, one of the following situations occurs:

(i) a donation point $i, i \in I$, is assigned to a BF $j, j \in J$, within the reachability threshold r (i.e., $x_{ij} = 1$). According to our hypotheses, we enforce the allocation of each donation point to its closest BF;

(ii) a donation point $i, i \in I$, is assigned to an MU transferring the collected blood to a BC $j, j \in J$, within the degradation threshold c_{max}. Here, two occurrences must be distinguished:

(a) the donation point i does not have any open BF (BS or BC) within the reachability threshold r. In this case, it is assigned to an MU transferring blood to an active BC within the degradation threshold c_{max} (i.e., $z_{ij} = 1$), and no closest assignment is enforced;
(b) the donation point i has at least an open BF (BS or BC) within the reachability threshold r. Let $k, k \in J$, be its closest BF. Under this circumstance, as assumed, all donors in i perform donations, and i should be assigned to k. However, to meet systems' requirements (e.g., maximum collection capacity at BFs), it can be assigned to an MU that transfers blood to an active BC (not necessarily the closest) within the degradation threshold c_{max} (i.e., $t_{ikj} = 1$);

(iii) a donation point remains unassigned.

Depending on the specific occurrence, donors contribute differently to the overall BSC accessibility. Specifically, donors falling in case (i) have to travel a distance $d_{ij} \leq r$ to reach the closest BF in j. Donors in (ii) give a null contribution: indeed, collection occurs directly at donors' points. As for (iii), donors in i should travel a distance $d_{ij} \geq r$ to reach a BF (and possibly donate blood). In view of this, we define additional auxiliary variables, denoted as $\overline{x}_{ij} = \{0,1\}$, $i \in I$ and $j, j \in J$, to compute the guaranteed accessibility of the system. Each of these variables assumes value 1 if the donation point i remains unassigned, but it is associated to a BF in j in the evaluation of the average accessibility.

Finally, the following four continuous non-negative decision variables are used:

- *Accessibility*
  - $l_i \geq 0$, $i \in I$: it computes the contribution of donors of location i to the average accessibility;
- *Self-sufficiency*
  - $\delta \geq 0$: it measures the scarcity of blood collection related to a given demand D;
- *Productivity and Capacity*
  - $\Phi_j \geq 0$ and $\Psi_j \geq 0$, $j \in J$: they represent the processed blood shortage and collection capacity overrun, respectively, at a BF location j.

For the sake of the clarity, the complete notation is summarized in Table 1.

To provide a clearer explanation of the introduced notation, we present an illustration of the BSC system under investigation and a feasible solution in Fig. 1, highlighting all the possible instance occurrences. Each donation point i, $i \in I$ is represented by a black dot, labeled with a letter ($i \in \{a, \dots, z\}$). Additionally, let us assume that each donation point is associated with the quantity of blood units given by the number in round brackets. Each potential facility location j, $j \in J$ is represented by gray geometrical figures, numbered from 1 to 5. Triangles represent facilities downgraded to BS (y^s_j variables equal to 1), squares represent facilities kept open as BC (y^c_j variables equal to 1), and circles represent closed facilities (y^c_j and y^s_j variables equal to 0). Two different covering areas – black and gray dashed line circles – are associated with each BF. These areas are built on the basis of the reachability threshold r and degradation threshold $c_{\max}$, respectively. Let us also consider the following parameter values: $D = 30$; $C = 10$ and $P_{\min} = 5$ for all the BFs. Finally, let us assume that all the penalties λ_1, λ_2 and λ_3 are set to very high values, but $\lambda_3 \gg \lambda_1$ and $\lambda_3 \gg \lambda_2$. This setting pushes towards solutions guaranteeing primarily the satisfaction of the regional self-sufficiency, secondarily the productivity and capacity requirements and, finally, the minimization of the system blood transportation costs. We observe that 4 BFs have to be opened to satisfy the regional blood demand D, so avoiding incurring in the resulting penalty. The red and green lines connect donation points with open BFs and they illustrate the x_{ij} and the z_{ij} assignment variables, respectively. Indeed, red straight lines are associated with donation points whose distanced from an open BF is within the reachability threshold r, while green straight lines are associated with donation points served by an MU, whose distanced from an open BF is larger than reachability threshold r but within the degradation threshold $c_{\max}$. Blue bold lines, connecting an open BS to an open BC whose mutual distances is within the degradation threshold $c_{\max}$, illustrate the $q_{jj'}$ transfer variables. Then, purple bold lines stand for the $t_{ijj'}$ transfer variables, and connect a donation point (o in Fig. 1), which should be inherently assigned to the nearest BF (3 in Fig. 1), to another open BF (4 in Fig. 1) by using an MU. Finally, brown dotted lines are related to $\overline{x}_{ij}$ variables, thus they connect an unassigned donation point to an open BF (likely the nearest one), to concur in the computation of the average accessibility. On the basis of the introduced picture legend, we can now easily explain the structure of the solution represented in Fig. 1. For the sake of comprehension, let us recall our assumption imposing that once a BF is open, every donation point within its reachability threshold must be assigned to the BF itself, or, in alternative, the blood of the donation point has to be collected by an MU and then transferred to another open BF within the degradation threshold. The BC located in 3 collects blood units from donation points h and i, so satisfying the imposed capacity limit and achieving the minimum productivity requirement. It also receives the blood collected from BS in 1, so increasing the amount of processed units. However, donation point j, which should be inherently assigned to BC 3, is instead assigned to BC 4 through the usage of an MU. The reason for this is that such blood transfer has a twofold positive effect. On the one hand, it avoids the violation of capacity constraints for BC 3 and, on the other hand, it allows the achievement of the productivity requirement for BC 4. Thus, no penalty is paid. Finally, BC in 5 meets the productivity requirement but it collects more blood than its capacity, thus incurring in the resulting penalty. The reason for this is that all the donation points within the reachability threshold of BC 5 can be assigned only to BC 5. To conclude, Fig. 1 allows also to show the evaluation of the average accessibility of the system. Indeed, it is computed summing the distance values d_{ij} associated with all the x_{ij} and $\overline{x}_{ij}$ variables equal to 1 (red and brown straight lines), then divided by $|I|$. A feasible solution has an accessibility lower than or equal to the threshold β.

Table 1
Notation used for the *BSC-MFLP* formulation.

Problem notation	
Sets and parameters:	
J	Set of potential BC/BS locations
I	Set of potential donors locations
α	Blood donation rate
p_i	Population of $i, i \in I$
a_i	Blood units collectable at i, $i \in I (a_i = \alpha p_i)$
d_{ij}	Distance between i and j, $i \in I \cup J, j \in J$
F	Maximum distance between a donor and a BC/BS ($F = max_{(i \in I, j \in J)} d_{ij}$)
r	Reachability threshold
$c_{\max}$	Degradation threshold
N_i	$\{j \in J \mid d_{ij} \leq r\}, \forall i \in I$
S_j	$\{i \in I \mid d_{ij} \leq r\}, \forall j \in J$
M_j	$\{j' \in J \mid d_{jj'} \leq c_{\max}\}, \forall j \in J$
O_i	$\{j \in J \mid d_{ij} \leq c_{\max}\}, \forall i \in I$
T_j	$\{i \in I \mid d_{ij} \leq c_{\max}\}, \forall j \in J$
D	Annual regional blood demand
$P_{\min}$	BC minimum productivity
C	BC/BS maximum collection capacity
β	Donor average accessibility distance
n	Number of available MUs
λ_1	Productivity shortage penalty
λ_2	Capacity overrunning penalty
λ_3	Blood self-sufficiency shortage penalty
Variables:	
$y_j^s \in \{0,1\}$	Equal to 1 a BS is open in $j, j \in J$, 0 otherwise
$y_j^c \in \{0,1\}$	Equal to 1 a BC is open in $j, j \in J$, 0 otherwise
$x_{ij} \in \{0,1\}$	Equal to 1 if donors located in $i, i \in I$, reach the BC/BS $j, j \in N_i$, 0 otherwise
$\overline{x}_{ij} \in \{0,1\}$	Auxiliary variable equal to 1 if donors in $i, i \in I$, are evaluated with respect to the open BC/BS $j, j \in J$, for the average accessibility
$q_{jj'} \in \{0,1\}$	Equal to 1 if blood collected in $j, j \in J$, is transferred in the BC j', $j' \in M_j$, to be processed, 0 otherwise
$z_{ij} \in \{0,1\}$	Equal to 1 if a MU collects blood of the donors located in $i, i \in I$, and transfers it to the BC $j, j \in O_i$, 0 otherwise
$t_{ijj'} \in \{0,1\}$	Equal to 1 if the donors located at $i, i \in I$, who could reach the open BC/BS located in $j, j \in N_i$, are served by a MU which transfers Blood to the BC $j', j' \in O_i$, 0 otherwise
$l_i \geq 0$	Auxiliary variable used to compute the contribution of donors located in $i, i \in I$ to the average accessibility
$\Phi_j \geq 0$	Processed blood shortage of the BC located in $j, j \in J$
$\Psi_j \geq 0$	Collection capacity overrunning of the BC/BS located in $j, j \in J$
$\delta \geq 0$	Scarcity of blood collection with respect to D

4.2. Mathematical formulation for BSC-MFLP-CB

Using the notation introduced in Section 4.1, the *BSC-MFLP-CB* can be formulated as follows:

$$Min \sum_{i \in I} \sum_{j \in N_i} \sum_{j' \in M_j} a_i d_{jj'} x_{ij} q_{jj'} + \sum_{i \in I} \sum_{j \in O_i} a_i d_{ij} z_{ij} + \sum_{i \in I} \sum_{j \in N_i} \sum_{j' \in O_i} a_i d_{ij'} t_{ijj'} + \sum_{j \in J} (\lambda_1 \Phi_j + \lambda_2 \Psi_j) + \lambda_3 \delta \quad (1)$$

$s.t.$

$$y_j^s + y_j^c \leq 1 \qquad \forall j \in J \quad (2)$$

$$x_{ij} + \sum_{j' \in O_i} t_{ijj'} \leq y_j^s + y_j^c \qquad \forall i \in I, j \in N_i \quad (3)$$

$$\sum_{k \in N_i} (x_{ik} + (\sum_{l \in O_i} t_{ikl})) \geq y_j^s + y_j^c \qquad \forall j \in J, i \in S_j \quad (4)$$

$$\sum_{j' \in N_i} d_{ij'} (x_{ij'} + \sum_{k \in O_i} t_{ij'k}) + (F - d_{ij})(y_j^s + y_j^c) \leq F \qquad \forall i \in I, j \in N_i \quad (5)$$

$$q_{jj'} \leq y_{j'}^c \qquad \forall j \in J, j' \in M_j^+ \quad (6)$$

$$\sum_{j' \in M_j^+} q_{jj'} = y_j^s + y_j^c \qquad \forall j \in J \quad (7)$$

$$q_{jj} \geq y^c_j \qquad \forall j \in J \quad (8)$$

$$\sum_{j\in N_i}(x_{ij} + \sum_{j'\in O_i} t_{ijj'}) + \sum_{j\in O_i} z_{ij} \leq 1 \qquad \forall i \in I \quad (9)$$

$$z_{ij} \leq y^c_j \qquad \forall i \in I, j \in O_i (10)$$

$$t_{ijj'} \leq y^c_{j'} \qquad \forall i \in I, j \in N_i, j' \in O_i (11)$$

$$\sum_{i\in I} a_i [\sum_{j\in N_i}(x_{ij} + \sum_{j'\in O_i} t_{ijj'}) + \sum_{j\in O_i} z_{ij}] + \delta \geq D \qquad (12)$$

$$\sum_{i\in S_j} a_i x_{ij} - \Psi_j \leq C \qquad \forall j \in J (13)$$

$$\sum_{k\in M^+_j}\sum_{i\in S_k} a_i x_{ik} q_{kj} + \sum_{i\in T_j} a_i (z_{ij} + \sum_{k\in N_i} t_{ikj}) + \Phi_j \geq P_{\min}\, y^c_j \qquad \forall j \in J (14)$$

$$\sum_{i\in I}\sum_{j\in O_i}(z_{ij} + \sum_{j'\in N_i} t_{ij'j}) \leq n \qquad (15)$$

$$\overline{x}_{ij} \leq y^s_j + y^c_j \qquad \forall i \in I, j \in J (16)$$

$$\sum_{j\in J}\overline{x}_{ij} + \sum_{j\in N_i}(x_{ij} + \sum_{j'\in O_i} t_{ijj'}) + \sum_{j\in O_i} z_{ij} = 1 \qquad \forall i \in I (17)$$

$$l_i \geq \sum_{j\in J} d_{ij}\overline{x}_{ij} + \sum_{j\in N_i} d_{ij} x_{ij} \qquad \forall i \in I (18)$$

$$\sum_{i\in I} l_i \leq \beta |I| \qquad (19)$$

$$y^c_j \in \{0,1\}, y^s_j \in \{0,1\} \qquad \forall j \in J (20)$$

$$x_{ij} \in \{0,1\} \qquad \forall i \in I, j \in N_i (21)$$

$$z_{ij} \in \{0,1\} \qquad \forall i \in I, j \in O_i (22)$$

$$q_{jj'} \in \{0,1\} \qquad \forall j \in J, j' \in M^+_j (23)$$

$$t_{ijj'} \in \{0,1\} \qquad \forall i \in I, j \in N_i, j' \in O_i (24)$$

$$l_i \geq 0 \qquad \forall i \in I (25)$$

$$\Phi_j \geq 0, \Psi_j \geq 0 \qquad \forall j \in J (26)$$

$$\delta \geq 0 \qquad (27)$$

The objective function (1) represents the overall system costs. In particular, the first three terms represent the weighted blood transportation cost. Specifically, the first term represents the BS-to-BC transportation costs if donors perform donations autonomously at BS ($\sum_{i\in I}\sum_{j\in N_i}\sum_{j'\in M_j} a_i d_{jj'} x_{ij} q_{jj'}$). The second and third terms refer to transportation costs for blood units collected by MUs ($\sum_{i\in I}\sum_{j\in O_i} a_i d_{ij} z_{ij}[\sum_{i\in I}\sum_{j\in N_i}\sum_{j'\in O_i} a_i d_{ij'} t_{ijj'}]$). The last two terms represent the penalties arising from the violation of the soft constraints: minimum productivity ($\sum_{j\in J}\lambda_1\Phi_j$); maximum collection capacity ($\sum_{j\in J}\lambda_2\Psi_j$); self-sufficiency ($\lambda_3\delta$). Constraints (2) ensure that a BF can be used either as a BC or as a BS. Constraints (3) are consistency constraints between assignment and location variables. They impose that donors can be assigned to a BF only if there is an open BS or BC. Constraints (4) ensure that if there is an open BF, the blood of all the donors located within the reachability threshold will be collected. Constraints (5), in combination with (4), guarantee that either a donation point is assigned to the nearest open BF within the reachability threshold (closest assignment) or it has to be served by an MU. More precisely, let us consider a generic donation point $i, i \in I$ and let j and $j', j, j' \in N_i$, be open BFs within the reachability threshold r. Moreover, let us assume that j' is the closest BF w.r.t. i. Because of Constraints (4), donation point i has to be mandatory assigned. Given Constraints (2), the following conditions hold: $y^c_j + y^s_j = 1$ and $y^c_{j'} + y^s_{j'} = 1$. On this basis, Constraints (5) either impose $x_{ij'} = 1$ or $t_{ij'k} = 1$, where $k, k \in O_i$, is a BC within the degradation threshold c_{max}. In the first case, closest assignment is imposed, while, in the second case, donations are collected at i by an MU and transferred to a BC in k, not necessarily the closest to j'. As discussed, such occurrence can help meeting specific system requirements (maximum collection capacity/accessibility). Constraints (6) ensure that blood collected in a BF is processed in an open BC. Constraints (7) impose that blood collected in a BF has to be transferred to a BC within the degradation threshold. Constraints (8) guarantee that blood collected in a BC will be processed by itself. Constraints (9) ensure that blood of each donation point can be collected at most once. These inequalities also establish a logical relationship between the x, t, and z variables, which is clarified in following of the section. Constraints (10) impose that MUs can transfer blood only to open BC. Constraints (11) guarantee that blood re-allocations can occur only in correspondence with an active BC. The soft constraint (12) ensures that the total amount of blood collected is at least equal to the regional blood demand D (self-sufficiency goal). Soft constraints (13) define an upper limit to the capacity for the collection activities at each facility. Soft constraints (14) require that blood processed in each BC satisfies the minimum productivity target P_{min}. Constraints (15) ensure that the total number of the MUs does not exceed the fleet size. Constraints (16)–(18) guarantee the consistency between donor assignment variables (x, t, and z) and the auxiliary variables ($\overline{x}$ and l) used to compute the average donor distance. In particular, Constraints (16) guarantee that the accessibility of unassigned donors' points is evaluated only w.r.t. open BFs. Constraints (17) guarantee that the accessibility of unassigned donation points is always computed. Finally, Constraints (18) compute the accessibility l_i of each donor point $i, i \in I$. Constraint (19) ensures that the average donor distance to an open BC/BS is smaller than the threshold β. Finally, constraints (20)–(27) concern the nature of the variables.

The model just described is not linear due to the product between the two decision variables x_{ij} and $q_{jj'}$ in the objective function (1) and constraints (14). However, as widely known, it is possible to linearize both terms by introducing a new binary decision variable $w_{ijj'}$ ($w_{ijj'} = x_{ij}q_{jj'}$) and the following set of constraints:

$$w_{ijj'} \leq x_{ij} \qquad \forall i \in I, j \in N_i, j' \in M_j^+ \quad (28)$$

$$w_{ijj'} \leq q_{jj'} \qquad \forall i \in I, j \in N_i, j' \in M_j^+ \quad (29)$$

$$w_{ijj'} \geq x_{ij} + q_{jj'} - 1 \qquad \forall i \in I, j \in N_i, j' \in M_j^+ \quad (30)$$

Constraints (28), (29) and (30) ensure that a binary variable $w_{ijj'}$ is equal to 1 if and only if donors located in $i, i \in I$, are assigned to the BS located in $j, j \in N_i$, and the collected blood is transferred and then processed in $j' \in M_j^+$. The objective function (1) and the constraints (14) will therefore be rewritten in the following form:

$$Min \sum_{i\in I}\sum_{j\in N_i}\sum_{j'\in M_j} a_i d_{jj'} w_{ijj'} + \sum_{i\in I}\sum_{j\in O_i} a_i d_{ij} z_{ij} + \sum_{i\in I}\sum_{j\in N_i}\sum_{j'\in O_i} a_i d_{ij'} t_{ijj'} + \sum_{j\in J}(\lambda_1 \Phi_j + \lambda_2 \Psi_j) + \lambda_3 \delta \quad (31)$$

$s.t.$

(2)–(13), (15)–(27)

$$\sum_{k\in M_j^+}\sum_{i\in S_k} a_i w_{ikj} + \sum_{i\in T_j} a_i (z_{ij} + \sum_{k\in N_i} t_{ikj}) + \Phi_j \geq P_{min}\ y_j^c \qquad \forall j \in J \quad (32)$$

We conclude this section providing a clarification on how the defined decision variables and the interrelationship among them align with the underlying assumptions of the described problem. To this end, let us consider a generic donation point $i, i \in I$, and only two open BFs, j and $j', j, j' \in O_i$ and $j' \neq j$, both located within the degradation threshold c_{max}. Without loss of generality, let j' be the closest facility to i, and let both facilities be BCs. The following cases may occur:

- **Case 1: Both BCs are located farther than r w.r.t. i (i.e., $j, j' \notin N_i$).** According to Constraints (3), donation point i cannot be assigned to any of the open BFs (x_{ij} and $t_{ijj'}$ variables are all equal to 0). Thus, if needed for self-sufficiency, the donations point i may be served only by an MU, delivering the collected blood to j or j' ($z_{ij} = 1$ or $z_{ij'} = 1$).
- **Case 2: Only BC j' is located within r w.r.t. i (i.e., $j' \in N_i, j \notin N_i$).** Constraints (3) and Constraints (4) impose that blood in i has to collected. Thus, either i must be assigned to its closest facility j' (i.e., $x_{ij'} = 1$) or served by an MU that would deliver blood to j or j' for processing (i.e., $t_{ij'j} + t_{ij'j'} = 1$). Under this circumstance, the z-variables are forced to be equal to zero.
- **Case 3: Both BCs are located within r w.r.t. i ($j, j' \in N_i$).** Due to Constraints (5), variables t_{ijj} and $t_{ijj'}$ will both be equal to zero since we assumed BC j' to be the closest to donor point i. Thus, Case 3 reduces to Case 2.

On the basis of this discussion, we observe that: t and z-variables cannot take value one simultaneously; variables $t_{ij'j}$ must be defined also for $j = j'$. Indeed, if the maximum collection capacity at the closest facility j' would be exceeded due to the amount of donations at i, such donations would be collected by an MU and delivered to j', thus only contributing to its processing activities. Alternatively, the model may decide to deliver these units to j. Such choice would depend on the transportation costs to be minimized and the need to meet minimum productivity requirements. In addition, we emphasize that the above example holds even if a BS was located at j'. In this case, variable $t_{ij'j'}$ would have been equal to zero due to Constraints (11). Therefore, in such a circumstance, either i is assigned to j' or to an MU that delivers its blood units at j.

4.3. Mathematical formulation for BSC-MFLP-SB

The donation rate α is a crucial parameter for the problem under investigation and it has shown a quite stable trend over the last years (Catalano et al., 2021). However, as discussed in Section 1, even small fluctuations can have significant impacts on the BSC operations. Thus, it represents an inherent source of uncertainty which deserves to be investigated by devising ad-hoc uncertainty based models which allow to design more robust BSC solutions.

Such situation configures a BSC-MFLP under uncertainty. We assume that uncertainty can be captured by a finite set of scenarios, say Π, where a "scenario" represents a full realization of the uncertain parameter α. Under this simplifying but widely known and used hypothesis (see, e.g., Correia and Saldanha-da Gama, 2019; Govindan et al., 2017), the BSC-MFLP can be modeled by a deterministic scenario-based equivalent formulation (BSC-MFLP-SB), by indexing in Π the donation rate parameter (α_π, $\pi \in \Pi$), and several decision-variables.

Specifically, we assume that only the strategic location-variables (i.e., y_j^c and y_j^s, $j \in J$) are scenario-independent decisions. Hence, a solution is sought which adapts to occurring scenarios by appropriately defining the donors-to-facilities allocations ($x_{ij\pi}$), the BSs-to-BCs assignments ($q'_{jj\pi}$), as well as the dispatching and use of MUs ($z_{ij\pi}$, $t_{ijj'\pi}$). Clearly, also the decision variables accounting for the violation of the main requirements (e.g., self-sufficiency, minimum productivity level, maximum collection capacity) are indexed in Π (δ_π, ψ_π, ϕ_π). The same applies to the auxiliary variables used for computing accessibility, which depend on scenario-dependent allocation decisions ($\overline{x}_{ij\pi}$, $l_{i\pi}$).

Finally, we also assume that the occurrence of scenarios $\pi \in \Pi$ can be measured probabilistically and we denote by ω_π such probabilities.

Two possible cases are considered, corresponding to two different decision-making attitudes towards risk: risk-neutral and risk-averse. Mathematically, we formulate them in terms of the minimization of the expected and maximum BSC's costs across the occurring scenarios, respectively. The goal is to provide additional evidence on the impact and the type of solutions that an uncertainty-aware decision-maker can evaluate as an alternative to classical sensitivity analysis. Using this additional notation (and that introduced in Section 4.1), the *BSC-MFLP-SB* model, in its linearized form, can be formulated as follows:

$$Min \sum_{\pi\in\Pi}\omega_\pi[\sum_{i\in I}\sum_{j\in N_i}\sum_{j'\in M_j} a_{i\pi}d_{jj'}w_{ijj'\pi} + \sum_{i\in I}\sum_{j\in O_i} a_{i\pi}d_{ij}z_{ij\pi} + \sum_{i\in I}\sum_{j\in N_i}\sum_{j'\in O_i} a_{i\pi}d_{ij'}t_{ijj'\pi} + \sum_{j\in J}(\lambda_1\Phi_{j\pi} + \lambda_2\Psi_{j\pi}) + \lambda_3\delta_\pi] \quad (33)$$

s.t.

$$y_j^s + y_j^c \le 1 \qquad \forall j \in J \quad (34)$$

$$x_{ij\pi} + \sum_{j'\in O_i} t_{ijj'\pi} \le y_j^s + y_j^c \qquad \forall i \in I, j \in N_i, \pi \in \Pi \quad (35)$$

$$\sum_{k\in N_i} x_{ik\pi} + (\sum_{l\in O_i} t_{ikl\pi}) \ge y_j^s + y_j^c \qquad \forall j \in J, i \in S_j, \pi \in \Pi \quad (36)$$

$$\sum_{j'\in N_i} d_{ij'}(x_{ij'\pi} + \sum_{k\in O_i} t_{ij'k\pi}) + (F - d_{ij})(y_j^s + y_j^c) \le F \qquad \forall i \in I, j \in N_i, \pi \in \Pi \quad (37)$$

$$q_{jj'\pi} \le y_{j'}^c \qquad \forall j \in J, j' \in M_j^+, \pi \in \Pi \quad (38)$$

$$\sum_{j'\in M_j^+} q_{jj'\pi} = y_j^s + y_j^c \qquad \forall j \in J, \pi \in \Pi \quad (39)$$

$$q_{jj\pi} \ge y_j^c \qquad \forall j \in J, \pi \in \Pi \quad (40)$$

$$\sum_{j\in N_i}(x_{ij\pi} + \sum_{j'\in O_i} t_{ijj'\pi}) + \sum_{j\in O_i} z_{ij\pi} \le 1 \qquad \forall i \in I, \pi \in \Pi \quad (41)$$

$$z_{ij\pi} \le y_j^c \qquad \forall i \in I, j \in O_i, \pi \in \Pi \quad (42)$$

$$t_{ijj'\pi} \le y_{j'}^c \qquad \forall i \in I, j \in N_i, j' \in O_i, \pi \in \Pi \quad (43)$$

$$\sum_{i\in I} a_{i\pi}[\sum_{j\in N_i}(x_{ij\pi} + \sum_{j'\in O_i} t_{ijj'\pi}) + \sum_{j\in O_i} z_{ij\pi}] + \delta_\pi \ge D \qquad \forall \pi \in \Pi \quad (44)$$

$$\sum_{i\in S_j} a_{i\pi}x_{ij\pi} - \Psi_{j\pi} \le C \qquad \forall j \in J, \pi \in \Pi \quad (45)$$

$$\sum_{k\in M_j^+}\sum_{i\in S_k} a_{i\pi}w_{ikj\pi} + \sum_{i\in T_j} a_{i\pi}(z_{ij\pi} + \sum_{k\in N_i} t_{ikj\pi}) + \Phi_{j\pi} \ge P_{min}\ y_j^c \qquad \forall j \in J, \pi \in \Pi \quad (46)$$

$$\sum_{i\in I}\sum_{j\in O_i}(z_{ij\pi} + \sum_{j'\in N_i} t_{ij'j\pi}) \le n \qquad \forall \pi \in \Pi \quad (47)$$

$$\overline{x}_{ij\pi} \le y_j^s + y_j^c \qquad \forall i \in I, j \in J, \pi \in \Pi \quad (48)$$

$$\sum_{j\in J}\overline{x}_{ij\pi} + \sum_{j\in N_i}(x_{ij\pi} + \sum_{j'\in O_i} t_{ijj'\pi}) + \sum_{j\in O_i} z_{ij\pi} = 1 \qquad \forall i \in I, \pi \in \Pi \quad (49)$$

$$l_{i\pi} \ge \sum_{j\in J} d_{ij}\overline{x}_{ij\pi} + \sum_{j\in N_i} d_{ij}x_{ij\pi} \qquad \forall i \in I, \pi \in \Pi \quad (50)$$

$$\sum_{i\in I} l_{i\pi} \le \beta|I| \qquad \forall \pi \in \Pi \quad (51)$$

$$y_j^c \in \{0,1\}, y_j^s \in \{0,1\} \qquad \forall j \in J \quad (52)$$

$$x_{ij\pi} \in \{0,1\} \qquad \forall i \in I, j \in N_i, \pi \in \Pi \quad (53)$$

$$z_{ij\pi} \in \{0,1\} \qquad \forall i \in I, j \in O_i, \pi \in \Pi \quad (54)$$

$$q_{jj'\pi} \in \{0,1\} \qquad \forall j \in J, j' \in M_j^+, \pi \in \Pi \quad (55)$$

$$t_{ijj'\pi} \in \{0,1\} \qquad \forall i \in I, j \in N_i, j' \in O_i, \pi \in \Pi \quad (56)$$

$$l_{i\pi} \ge 0 \qquad \forall i \in I, \pi \in \Pi \quad (57)$$

$$\Phi_{j\pi} \ge 0, \Psi_{j\pi} \ge 0 \qquad \forall j \in J, \pi \in \Pi \quad (58)$$

$$\delta_\pi \ge 0 \qquad \forall \pi \in \Pi \quad (59)$$

For the sake of brevity, we do not provide a discussion of the model, since the explanation of the constraints follows that given for the *BSC-MFLP-CB* formulation. We just highlight that the objective function (33) minimizes the expected value of the system costs over all the scenarios weighted by the corresponding occurrence probability ω_π.

The proposed *BSC-MFLP-SB* formulation can be slightly modified to minimize the worst-case scenario by varying the objective function, as follows:

$$Min\ Max_{\pi\in\Pi}\ [\sum_{i\in I}\sum_{j\in N_i}\sum_{j'\in M_j} a_{i\pi} d_{jj'} w_{ijj'\pi} + \sum_{i\in I}\sum_{j\in O_i} a_{i\pi} d_{ij} z_{ij\pi} + \sum_{i\in I}\sum_{j\in N_i}\sum_{j'\in O_i} a_{i\pi} d_{ij'} t_{ijj'\pi} + \sum_{j\in J}(\lambda_1 \Phi_{j\pi} + \lambda_2 \Psi_{j\pi}) + \lambda_3 \delta_\pi] \quad (60)$$

$s.t.$

(34)–(59)

Objective function (60) configures a *minmax* problem that, as widely known, can be easily linearized replacing the objective function by an additional non-negative continuous decision variable and introducing bounding constraints. In the following, for the sake of readability, we denote the expected value and worst-case versions of the *BSC-MFLP-SB* as *BSC-MFLP-SB*$_{sum}$ and *BSC-MFLP-SB*$_{max}$, respectively.

4.4. MILP formulation enhancements

This section is devoted to present enhancements of the proposed MILP formulations in order to strengthen the linear relaxation and improve the overall computational efficiency. Upon examining constraints (5) and (37) for the *BSC-MFLP-CB* and *BSC-MFLP-SB* formulations, respectively, we observe that the usage of F configure a set of $bigM$ constraints in each model. As widely known, this can result in numerical instability and weaker formulations. Such drawback can be partially overcome by a constraint reformulation. For the sake of comprehension, since the extension to the *BSC-MFLP-SB* formulation is straightforward, our discussion is focused only on the *BSC-MFLP-CB* formulation. Constraints (5) are conceived as closest assignment constraints where the introduction of a $bigM$ is needed to make the constraint ineffective in case no BF is open either within the reachability threshold or within the degradation distance of a donation point. We can reformulate these constraints as follows:

$$\sum_{j\in N_i | d_{ij} > d_{ik}} x_{ij} + \sum_{h\in O_i | d_{il} > d_{ik}} t_{ilh} \le 1 - (y_k^s + y_k^c) \qquad \forall i \in I, k \in N_i, l \in N_i \quad (61)$$

Given a donation point i, $i \in I$, the constraints (61) still allow to obtain a closest assignment by introducing a distance-based ordering of the BFs belonging to N_i and the ones belonging to O_i. Specifically, they set to zero all the assignment variables related to BFs that are not the closest to a donation point. Such reformulation leads to a strengthened linear relaxation of the *BSC-MFLP-CB* model and are used in the following computational analysis. Finally, the following set of valid inequalities can be derived from the problem structure:

$$y_j^s \le \sum_{i\in M_j} y_i^c \qquad \forall j \in J \quad (62)$$

These inequalities impose that, given a BF location j, $j \in J$, we cannot have a BS in j if no BC is open within the degradation threshold, i.e., the set M_j is empty. The proof of these inequalities is straightforward. Indeed, let us consider a location $\hat{j}$ whose set $M_{\hat{j}}$ is empty. We can easily verify that a fractional solution with both values $\hat{y}_j^s$ and $\hat{y}_j^c$ higher than 0, satisfy all the constraints linking these variables each other and with the transfer variables $q_{jj'}$, namely constraints (6), (7) and (8), but it does not satisfy the constraints (62). The constraints (62), involving only location variables, can be directly added also to the *BSC-MFLP-SB* formulation. Instead, the constraints (61) can be tailored for the *BSC-MFLP-SB* model by extending them to all the scenarios in π, $\pi \in \Pi$, as follows:

$$\sum_{j\in N_i | d_{ij} > d_{ik}} x_{ij\pi} + \sum_{h\in O_i | d_{il} > d_{ik}} t_{ilh\pi} \le 1 - (y_k^s + y_k^c) \qquad \forall i \in I, k \in N_i, l \in N_i, \pi \in \Pi \quad (63)$$

5. Experimental results

In this section, we test and validate the proposed MILP formulations on real cases related to three Italian regions, namely Campania, Lombardy and Apulia. We selected these regions because they present different geographical/topological and demographic features. Specifically:

1. Campania has a “compact” shape (i.e., it is somehow “rounded”, that is, not very elongated or undistorted); Lombardy is one of the most widely extended regions in Italy; Apulia develops mainly longitudinally (i.e., its shape is not as compact as Campania);
2. Lombardy and Campania are the first two Italian regions for population density, mainly concentrated in densely inhabited urban areas; the population of Apulia, instead, even if high, is more evenly distributed between urban and rural areas.

Section 5.1 describes the instance generation and parameter setting. Sections 5.2–5.4 are devoted to the presentation and discussion of the experimental results obtained for each region.

5.1. Instance generation and parameter setting

The *BSC-MFLP* requires the definition of the donor locations (I) and potential blood facility (J) sets. Concerning the first set, we exploit the pre-existing municipalities constituting the regional territory, which have known populations (p_i), obtained using the latest consolidated census data according to the Italian National Statistics Institute—ISTAT. The number of donor locations (i.e., the cardinality of I) is 559, 257, and 1513 for the Campania, Apulia, and Lombardy regions, respectively (ISTAT, 2011). Their positions are assumed to correspond to the centroids of the municipalities and are extracted using the open-source GIS software QGIS. Following previous studies on the topic, we assume a uniformly distributed donation rate (α) across each municipality, with all donors located at their respective centroids (Bruno et al., 2019). For regions with larger populations, such as Campania and Lombardy, the municipalities of Naples and Milan are each subdivided into ten sub-areas to effectively manage the high number of inhabitants. The donation rate is assumed to be equal across all the municipalities and its value is determined based on historical data provided by the regional authority. On average, it has been observed that nearly 50 donations per 1000 inhabitants have been made in Italy over the past five years (Catalano et al., 2021), thus setting $\alpha = 0.05$. Moreover, in order to simulate the effects of potential regional campaigns of awareness aimed at increasing the propensity of the population to blood donation, or the decrease of this rate aimed at simulating a stressful situation for regional blood management system, we also considered the cases with $\alpha = 0.06$ and $\alpha = 0.04$, respectively. We assume that each donor performs one donation per year, thus, the number of donated units for each areas is given by αp_i. The *BSC-MFLP-CB* formulation has been evaluated considering singularly the three chosen donation rate values. Instead, the *BSC-MFLP-SB* formulation has been evaluated considering simultaneously the three donation rate values, i.e., $\alpha_1 = 0.04$, $\alpha_2 = 0.05$ and $\alpha_3 = 0.06$, imposing $\omega_1 = 0.25$, $\omega_2 = 0.5$ and $\omega_3 = 0.25$, respectively. Such values are coherent with the minimal fluctuations observed in blood donations (Catalano et al., 2021).

The values of the annual regional blood demands (D), have been set equal to 161,360 for Campania, 163,881 for Apulia and 470,770 for Lombardy (Catalano et al., 2021).

Concerning the potential BF set, we consider the number and the position of the existing blood centers in each region, i.e., 22, 21 and 33 BCs in Campania, Apulia and Lombardy, respectively. The P_{min} value is fixed to 40.000 units for all the BCs, according to the imposed EU and Italian regulation. We highlight that all the three regions have an average level of productivity significantly lower than the minimum productivity, in particular: 7335 units for Campania (161,360 donations in 22 BCs); 7804 units for Apulia (163,881 donations in 21 BCs); 14,265 for Lombardy (470,770 donations in 33 BCs). Consistently with the productivity value, for all the BFs, the capacity value C is assumed to be equal to 50.000 units.

All the required distances, d_{ij} and $c_{jk}, i \in I, j, k \in J$, were calculated as the shortest paths on the road network. Concerning the other used modeling parameters, r and c_{max} are set equal to 20 km and 50 km, respectively. We recall that c_{max} is the maximum distance value between two fixed facilities or a mobile unit and a fixed facility. The number of MUs is equal to 20 (see AVIS, 2021).

Finally, a discussion is needed about the setting of the average accessibility threshold and the penalty parameters in the objective function. In particular:

1. Four different values have been used for the accessibility threshold β: 15, 40, 45 and 60 km. These values allow to simulate different accessibility configurations.
2. Four different values of the penalty linked to the non-compliance with the efficiency requirements (minimum productivity), λ_1: 0, 1, 10 and 100.
3. Four different values of the penalty linked with the overrunning of the maximum collection capacity, λ_2: 0, 1, 10 and 100.
4. A single very large value for the penalty linked to the self-sufficiency requirement, $\lambda_3 = 10^6$.

The main idea behind the chosen setting of the penalty values is that the reorganization process of the BSC cannot be an abrupt and binary shift from the current state to the final solution because of work force management and process re-engineering. Instead, it needs to happen gradually over a period of time. This entails initially closing or reconverting certain BCs and progressively moving towards the desired end goal. According to the Italian guidelines, the primary objective is to ensure self-sufficiency, while it is acceptable to temporarily violate the capacity and productivity constraints, considering that a complete system reconfiguration cannot be achieved within a very short time-frame. On this basis, we fixed a very high value for λ_3 and lower but increasing values for λ_1 and λ_2, which have been empirically defined. The chosen penalty values, in combination with the other calibration parameters, enable the evaluation of both the individual and combined effects on the attainable solutions. Additionally, they provide managerial insights to the decision-maker during the gradual reorganization of the regional BSC.

Finally, we highlight that the proposed model can be used with a twofold perspective:

1. A *centralized strategy*, which considers a region as a single block;
2. A *decentralized strategy* which divides a region in areas, each of them including one or more cities and related municipalities.

The decentralized strategy is advisable in cases where there is a city which acts as a gravity center polarizing the solution, as it occurs in Campania region where the inhabitants of the area of Naples constitute about 50% of the whole population. Thus, for the Campania region, we experience also the decentralized strategy dividing the municipalities in two blocks, the first including the areas of Naples and Caserta, the second including the areas of Salerno, Benevento and Avellino.

Therefore, summarizing, considering the combinations of all the tuning parameters, we performed the following experimentation:

- 48, 16 and 16 instances of the *BSC-MFLP-CB*, *BSC-MFLP-MS*$_{sum}$ and *BSC-MFLP-SB*$_{max}$, respectively, with centralized strategy for each region;

- 48 instances of the *BSC-MFLP-CB* with decentralized strategy in Campania.

Each instance is defined by the combination of the parameters considered and by the following encode: $Region_{ID}\_\lambda_1\_\lambda_2\_\beta$. The used $Region_{ID}$ are: C for Campania; P for Apulia; L for Lombardy.

All the instances have been run on an Intel Core i7, 2.60 GHz, 16.00 GB RAM, using Gurobi 9.0.1 as MILP solver. All the *BSC-MFLP-CB* instances have been solved to optimality within 600 s. The two variants of the *BSC-MFLP-SB* require a higher computational effort, between 2 and 4 h on average. For the sake of brevity, given the focus of the work on the specific real problem under investigation, we do not go into details concerning the computational aspects. However, we highlight that, the optimal solution is typically found within approximately 20% of the total computational time. Then, a considerable portion of the computational effort, approximately 80%, is expended mainly in narrowing the optimality gap.

The results for *BSC-MFLP-CB* are consolidated in tables that provide detailed information including: the instance ID (column 1); the donation rate (α — column 2); the transportation component of the objective function (column 3), calculated excluding the penalty component of the objective function and denoted as *Obj*; the values of Φ_{tot}, Ψ_{tot} (columns 4 and 5); δ (column 6), which represents the difference between the quantity of blood collected and the annual regional blood demand (D); the count of open BCs and BSs (#BCs, #BSs — columns 7 and 8); and lastly, the computation time (in seconds — column 12).

A more comprehensive discussion is warranted for indicators Φ_{tot} and Ψ_{tot}. Specifically, they are computed as: $\Phi_{tot} = \sum_{j\in J} \Phi_j$ and $\Psi_{tot} = \sum_{j\in J} \Psi_j$. Hence, Φ_{tot} represents the cumulative difference between the minimum productivity level (P_{min}) and the actual number of blood units processed by each center. Meanwhile, Ψ_{tot} reflects the aggregate of blood units exceeding the maximum capacity (C) set for each center. In practice, these indicators inform on the compliance of the obtained solutions w.r.t. productivity and collection capacity requirements.

Similar tables are used for the results of the *BSC-MFLP-SB* instances. In particular, they report: the instance ID (column 1); the objective function used, i.e., expressions (33) and (60), corresponding to formulations *BSC-MFLP-SB*$_{sum}$ and *BSC-MFLP-SB*$_{max}$, respectively (column 2); the transportation cost component of the objective function (*Obj* — column 3); then, the rest of the indicators already presented for the *BSC-MFLP-CB* tables follow (i.e., Φ_{tot}, Ψ_{tot}, δ, #BCs, #BSs). Note that, for the *BSC-MFLP-SB*$_{sum}$ case (i.e., the upper half of the tables), those indicators are calculated as the average across the set of scenarios (e.g., $\Phi_{tot} = \frac{1}{|\Pi|} \sum_{\pi\in\Pi} \sum_{j\in J} \omega_{pi}\Phi_{jw}$). Instead, the same indicators are expressed by their worst-case values for the *BSC-MFLP-SB*$_{max}$.

We report that, to enhance readability, the values in columns 3, 4, 5, and 6 have been scaled down by a factor of 1000 for both the *BSC-MFLP-CB* and the *BSC-MFLP-SB*.

Moreover, for some selected instances, we also provide a graphical representation of the obtained solutions, using the following graphical objects:

1. red dots for the centroids of each municipality;
2. yellow dots and blue squares for the open BCs and BSs, respectively, in the obtained solutions;
3. black, blue and red links for the donor-to-BF assignments (x-variables), donor-to-MU assignments (z-variables), and BS-to-BC assignments (q-variables), respectively;
4. yellow links for the re-allocation of a donor location between two different facilities.

Such representations allow to easily catch the effect of the topology on the number and type of open BFs (i.e., BS or BC).

5.2. Experimental results for Campania region

This section is devoted to Campania region and it is structured in three subsections: Section 5.2.1 containing the results of the *BSC-MFLP-CB* with centralized strategy; Section 5.2.2, devoted to the results of the *BSC-MFLP-CB* with decentralized strategy; finally, Section 5.2.3 concerning the results of the *BSC-MFLP-SB* variants.

5.2.1. Results of *BSC-MFLP-CB* -centralized strategy

In Table 2 we report the results of the experimentation for the centralized strategy of the Campania region varying the value of α, the value of β and the penalty values λ_1, λ_2. Two main trends emerge, the first related to productivity and capacity requirements, the second related to the accessibility.

Concerning the first trend, we observe that the number of BFs on the territory is largely influenced by the penalty parameters λ_1, λ_2 and the accessibility threshold β. Indeed, at equal values of β, the number of located BFs decreases as λ_1 and λ_2 increase. Recall that the latter parameters are representative of the decision-maker's sensitivity to minimum productivity and maximum collection capacity requirements. Therefore, to ensure compliance, the model pushes for a lower number of active BFs, which results in increased productivity values per BC. Notably, to this end, the possibility to downgrade active BCs in BSs is also successfully exploited. For instance, for $\alpha = 0.04$, the solution obtained for the C_0_0_15 instance (the first row in the table) has 18 BCs, which reduce to 12 for the C_100_100_15 case. The latter, however, are distinguished in four BCs and eight BSs, so that the productivity requirements are met ($\Phi_{tot} = 0$). Similar considerations apply for the other values of α. Besides, in terms of collection capacity, two main aspects emerge. First, the resulting overruns (reported under the Φ_{tot} column) are generally lower w.r.t. to capacity shortages, even when the corresponding penalty λ_2 equals zero. This is clear since the located BFs perform collection, which naturally makes this goal easier to accomplish. Second, resorting to MUs becomes a viable option when penalty increases. Indeed, the Obj column in the table reveals that any transportation cost greater than zero indicates one of two scenarios: either the utilization of MUs to transfer

Table 2
Results of *BSC-MFLP-CB* for Campania region: centralized strategy.

Instance (C_λ_1_λ_2_β)[a]	α	Obj	Φ_{tot}	Ψ_{tot}	δ	#BCs	#BSs	time (s)
C_0_0_15	0.04	0.00	513.87	0.00	0	18	0	34
C_0_0_30		0.00	443.75	0.00	0	16	0	30
C_0_0_45		0.00	188.03	11.47	0	8	0	29
C_0_0_60		0.00	375.10	0.00	0	14	0	26
C_1_1_15		432.68	181.38	0.00	0	9	0	70
C_1_1_30		0.00	57.21	0.00	0	5	0	130
C_1_1_45		0.00	18.83	0.00	0	4	0	119
C_1_1_60		0.00	18.83	0.00	0	4	0	86
C_10_10_15		432.68	66.46	0.00	0	6	3	98
C_10_10_30		78.63	29.22	1.06	0	4	1	206
C_10_10_45		93.32	0.00	0.32	0	3	1	123
C_10_10_60		93.32	0.00	0.32	0	3	1	111
C_100_100_15		2492.18	0.00	0.00	0	4	8	327
C_100_100_30		687.36	0.00	0.00	0	3	4	567
C_100_100_45		111.80	0.00	0.00	0	3	1	595
C_100_100_60		111.80	0.00	0.00	0	3	1	364
C_0_0_15	0.05	0.00	337.35	60.35	0	13	0	31
C_0_0_30		0.00	167.97	69.97	0	6	0	106
C_0_0_45		0.00	167.97	69.97	0	6	0	101
C_0_0_60		0.00	167.97	69.97	0	6	0	102
C_1_1_15		520.00	169.56	0.12	0	10	0	79
C_1_1_30		5.73	36.18	0.00	0	6	0	121
C_1_1_45		0.00	0.00	0.59	0	4	0	90
C_1_1_60		0.00	0.00	0.59	0	4	0	80
C_10_10_15		520.00	60.66	0.00	0	7	3	239
C_10_10_30		77.78	21.31	0.00	0	5	1	194
C_10_10_45		0.00	0.59	0.00	0	4	0	113
C_10_10_60		0.00	0.59	0.00	0	4	0	134
C_100_100_15		2349.45	0.01	0.00	0	6	7	340
C_100_100_30		536.47	0.00	0.00	0	5	2	338
C_100_100_45		15.88	0.00	0.00	0	4	1	115
C_100_100_60		15.88	0.00	0.00	0	4	1	179
C_0_0_15	0.06	0.00	233.07	79.97	0	11	0	28
C_0_0_30		0.00	433.27	13.53	0	17	0	32
C_0_0_45		0.00	221.25	87.80	0	9	0	30
C_0_0_60		0.00	293.84	12.32	0	13	1	36
C_1_1_15		393.27	136.52	5.44	0	10	0	84
C_1_1_30		0.00	39.19	0.79	0	7	0	124
C_1_1_45		0.00	0.00	6.69	0	5	0	123
C_1_1_60		0.00	0.00	6.69	0	5	0	93
C_10_10_15		393.27	61.88	0.00	0	8	3	190
C_10_10_30		65.44	17.57	1.58	0	6	2	145
C_10_10_45		13.77	0.00	0.00	0	5	2	93
C_10_10_60		13.77	0.00	0.00	0	5	2	126
C_100_100_15		1980.41	0.01	0.00	0	7	7	270
C_100_100_30		471.96	0.02	0.00	0	6	3	185
C_100_100_45		13.77	0.00	0.00	0	5	2	148
C_100_100_60		13.77	0.00	0.00	0	5	2	128

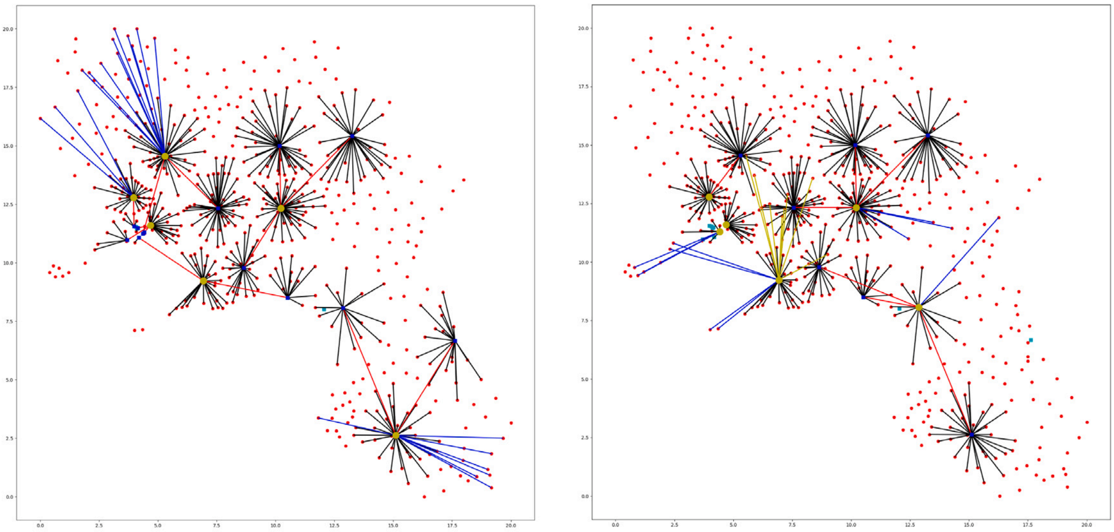
[a] *C* — Campania; λ_1 — minimum productivity penalty; λ_2 — maximum collection capacity penalty; β — accessibility threshold.

blood from BSs to BCs, or the servicing of several donor locations by MUs for collection. To gain a more detailed understanding of how MUs are utilized, readers are directed to the supplementary table 9 located in the appendix of this work.

In addition, the joint effect of penalties and accessibility on the number of located BFs is significant. In particular, for $\alpha = 0.04$, we can observe that, increasing the penalty values, the number of open BFs on the regional territory varies from 18 BCs (solution of C_0_0_15 characterized by large Φ_{tot} value) to just 4 open BFs, one BS and three BCs (solution of C_100_100_60, characterized by no productivity penalty).

Interestingly, the impact of the donation rate α also yields some intriguing findings. In general, as evidenced in previous works (e.g., Bruno et al., 2019), higher donation rates allow for stronger rationalization actions, that is, massive reduction of located BFs. This is only partially true in our case. Indeed, we often see that higher values of α (especially 0.06) lead to more facilities kept open (all other conditions being equal). Although apparently counter-intuitive, this strategic choice becomes necessary to comply with the maximum collection capacity constraints.

Concerning the second trend, we observe that higher accessibility thresholds β (that is, worse accessibility conditions for potential donors), yields a lower number of located BFs. We underline that accessibility is not explicitly discussed in the Italian decree. However, it should be seriously taken into account since it can discourage donations because of the high resulting traveling distances



(a) Centralized solution (b) Decentralized solution

Fig. 2. Comparison of centralized and decentralized strategy *BSC-MFLP-CB* solutions for the Campania region (C_100_100_15 instance, $\alpha = 0.05$)

to reach an open BF. From our results, it is also possible to note that $\beta = 45$ km is a critical accessibility threshold beyond which the solution does not vary almost for all the instances.

We highlight that using maximum values for λ_1 and λ_2 and fixing $\beta = 15$ km, regardless of the donation rate (C_100_100_15) the obtained solutions respect the EU and Italian regulation in terms of productivity. Such solutions, in practice, guarantee the same average accessibility threshold than the current situation, by resorting to the use of MUs (see table 9 in the appendix).

The above observations highlight, once more, the inherent multi-objective nature underlying our problem. Nevertheless, looking at the table, we observe that, using penalty values equal to 10, accepting accessibility values higher than 30, and regardless of the donation rate, we can achieve many solutions which open no more than 7 BFs (exploiting both BCs and BSs) providing very small and acceptable values for both Φ_{tot} and Ψ_{tot}. Thus, the obtained BSC configurations represent good trade-off solutions with respect to the conflicting objectives of the *BSC-MFLP*.

In other words, if accessibility is not an issue, compliance with the system's requirements (self-sufficiency, minimum productivity, and maximum collection) can be obtained together with significant savings in terms of open BFs. Nevertheless, as our results show, this requires taking ad-hoc decisions regarding BCs downgrading to BSs and a fairly limited dispatching of MUs.

Instead, if accessibility is also envisaged, compliance may not be always guaranteed. Moreover, the achievement of very strict accessibility thresholds would result in a relatively high number of located BFs (that is, less cost-effective rationalization actions) and a more intense involvement of MUs.

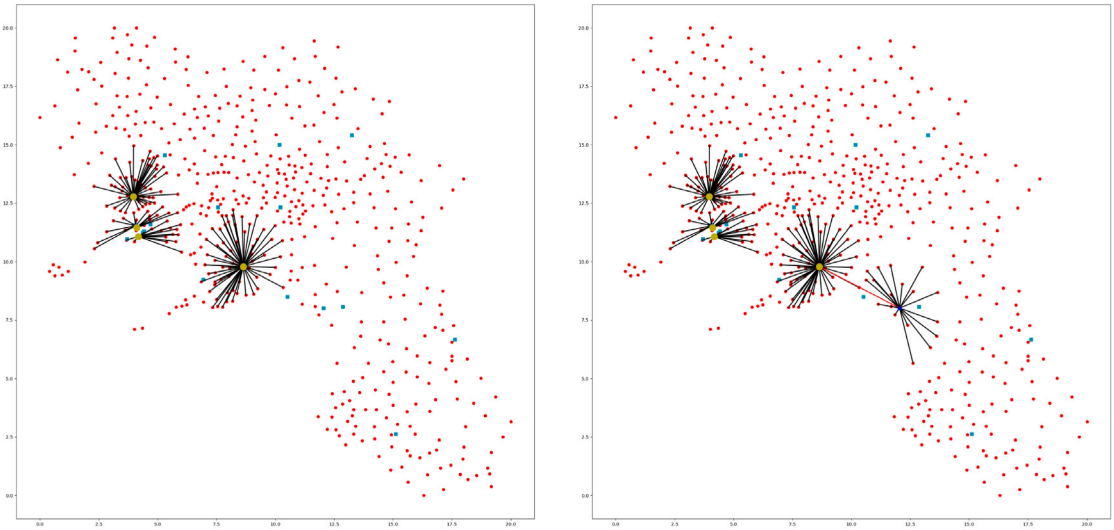
5.2.2. *Results of BSC-MFLP-CB-decentralized strategy*

The results of the decentralized strategy are reported in Table 3. The obtained trends are similar to those observed in the centralized strategy, but, as expected, the number of open BFs, on average, is higher (a minimum of 4 BFs for the centralized strategy and 5 BFs for the decentralized strategy).

In order to better show the difference between the strategies, in the following we provide the graphical representation of some achieved solutions.

In particular, we show the solutions of the C_100_100_15 instance for both the strategies (centralized vs. decentralized) in Figs. 2(a) and 2(b), respectively. These instances consider the same donation rate of the "as-is" situation ($\alpha = 0.05$) and guarantee the same average accessibility threshold ($\beta = 15$ km). We chose the highest values of the penalty parameters to comply with the decree. In this case it is easy to see that, with a low value of average accessibility threshold, the centralized and decentralized strategies converge to similar solutions. Indeed, in both instances, we have 13 BFs left open (6 BCs and 7 BSs) out of 22 on the regional territory.

Figs. 3(a) and 3(b) show the solutions of the instance C_100_100_45, with the centralized and decentralized strategies, respectively. These instances are characterized by $\beta = 45$ km (i.e., a higher accessibility threshold), and the same parameter settings as above. We observe that in the centralized strategy, 5 BFs are open (4 BCs and 1 BS), while in the decentralized strategy, an additional BS is used. Moreover, in the centralized strategy all the facilities are mainly located in the area of Naples which acts as "gravity center". This solution, even though respecting the decree, is a good solution in terms of cost saving but it turns out to be penalizing for all the population in the southern and eastern areas of the region. The decentralized strategy mitigates this effect by providing a slightly more expensive – but less polarized – solution.



(a) Centralized solution (b) Decentralized solution

Fig. 3. Comparison of centralized and decentralized strategy *BSC-MFLP-CB* solutions for Campania region (C_100_100_45 instance, $\alpha = 0.05$)

Similar considerations can be drawn by looking at the whole set of performed experiments.

In summary, we can conclude that if accessibility is sought (that is, low threshold values for parameter β are imposed), no significant differences are devised depending on the chosen strategy (centralized or decentralized). Instead, if accessibility is not a primary issue (that is, higher threshold values are set), decentralized strategies can be winning, as they yield solutions characterized by a higher and more widespread distribution of BFs over the territory. In a nutshell, we can say that the decentralized strategy is, in some sense, more *equity-oriented*, since higher "coverage" of the population is obtained by reducing the concentration effect determined by large and populated cities.

In our opinion, this is an interesting point which stimulates a reflection on effective BSC management taking into account geographical inequalities in access. However, it has to be noted that the strategic organization of regional BSCs in Italy is not delegated to local authorities (e.g., at the provincial or health districts level), and is not driven by explicit accessibility and equity considerations. For these reasons, in the following, we validate the *BSC-MFLP-SB* focusing only on the centralized strategy.

5.2.3. Results of *BSC-MFLP-SB*

Table 4 summarizes the results of *BSC-MFLP-SB*$_{sum}$ and *BSC-MFLP-SB*$_{max}$, respectively, with the centralized strategy. For the sake of brevity, we do not provide a discussion on the effects of the penalty and average accessibility threshold values, since it would be consistent with the case-based formulation. Thus, we focus only on the differentiating aspects between the two variants of the *BSC-MFLP-SB* (i.e., the expected and worst-case scenario versions — *BSC-MFLP-SB*$_{sum}$ and *BSC-MFLP-SB*$_{max}$, respectively) and between the case-based and scenario-based solutions. Concerning the two variants of the *BSC-MFLP-SB*, we can observe that, except few cases, we obtain similar (or even the same) solutions in terms of the number of located BFs. As expected, for some particular instances (e.g., with λ_1 and λ_2 equal to 0 and/or low values of β), the number of BFs open using the *BSC-MFLP-SB*$_{max}$, as well as the transportation cost component of the objective function, are higher. This is consistent with the proposed formulation, which returns a conservative solution by looking at worst-case scenario occurrence. Nevertheless, for most of the tested instances, no significant differences are devised. This finding denotes the robustness of the proposed solutions to the variation of the donation rate α, regardless of the decision-maker aptitude towards risk.

Regarding the comparison with the case-based formulation, it is important to note that our analysis specifically focuses only on the number of open BFs. This choice has a twofold motivation. Firstly, the intricate interplay and mutual influence of the different objective function components, induced by the selected penalty values, complicates a component-wise comparative analysis, making it challenging to interpret the results clearly and directly. Secondly, aligning with the real application, the main target is rationalizing the blood collection and processing activities of the BSC, closing or reconverting existing facilities. Based on this reasoning, we choose not to include scenarios where λ_1 and λ_2 are equal to 0. In such cases, the number of open BFs determined by the formulations could be misleading. In the following, for the sake of clarity, we denote as $BF-CB_{low}$ and $BF-CB_{high}$, the lowest and the highest number of BFs, respectively, returned by the *BSC-MFLP-CB* with the three considered donation rates. For Campania region $BF-CB_{low}$ and $BF-CB_{high}$ correspond to $\alpha = 0.04$ and $\alpha = 0.06$, respectively. As we expected, the *BSC-MFLP-SB*$_{sum}$ formulation provides good compromise solutions with respect to those obtained by the *BSC-MFLP-CB*. Indeed, when all conditions are identical, the number of BFs open in the *BSC-MFLP-SB*$_{sum}$ solution falls within the range defined by $BF-CB_{low}$ and $BF-CB_{high}$. For instance, let us consider the results of the instance C_100_100_15. We can observe that the *BSC-MFLP-SB*$_{sum}$ formulation locates 13 BFs (5 BCs and 8 BSs),

Table 3
Results of *BSC-MFLP-CB* for Campania region: decentralized strategy.

Instance (C_λ_1_λ_2_β)[a]	α	Obj	Φ_{tot}	Ψ_{tot}	δ	#BCs	#BSs	Time (s)
C_0_0_15	0.04	1.94	557.91	0.00	0	19	0	11
C_0_0_30		0.00	367.06	0.00	0	14	0	11
C_0_0_45		0.00	391.95	0.00	0	14	0	11
C_0_0_60		0.00	327.74	0.00	0	13	0	11
C_1_1_15		765.51	246.20	0.00	0	11	0	11
C_1_1_30		2.17	99.82	0.82	0	6	1	11
C_1_1_45		2.17	99.46	0.82	0	6	1	11
C_1_1_60		2.17	99.46	0.82	0	6	1	11
C_10_10_15		765.51	89.38	0.00	0	7	4	11
C_10_10_30		386.95	27.78	0.82	0	4	3	11
C_10_10_45		281.28	28.86	0.82	0	4	2	11
C_10_10_60		281.28	28.86	0.82	0	4	2	11
C_100_100_15		2894.33	2.61	0.00	0	5	7	11
C_100_100_30		955.98	0.00	0.00	0	3	7	10
C_100_100_45		666.63	0.00	0.00	0	3	5	11
C_100_100_60		666.63	0.00	0.00	0	3	5	11
C_0_0_15	0.05	5.19	473.48	0.00	0	18	0	11
C_0_0_30		0.00	367.25	5.97	0	15	0	11
C_0_0_45		0.00	238.58	3.40	0	11	0	11
C_0_0_60		0.00	373.66	0.12	0	15	0	10
C_1_1_15		552.96	217.74	11.94	0	11	0	11
C_1_1_30		0.00	88.27	0.59	0	7	0	11
C_1_1_45		0.00	54.51	0.59	0	6	0	11
C_1_1_60		0.00	54.51	0.59	0	6	0	11
C_10_10_15		552.96	82.28	0.12	0	8	4	11
C_10_10_30		480.98	24.73	0.59	0	5	2	11
C_10_10_45		0.00	27.88	0.59	0	5	0	11
C_10_10_60		0.00	27.88	0.59	0	5	0	11
C_100_100_15		2969.80	0.17	0.00	0	6	7	12
C_100_100_30		888.58	0.00	0.00	0	4	4	11
C_100_100_45		481.16	0.00	0.00	0	4	2	11
C_100_100_60		354.09	0.00	0.00	0	4	2	10
C_0_0_15	0.06	0.00	426.75	4.99	0	18	0	10
C_0_0_30		0.00	323.56	12.32	0	14	0	11
C_0_0_45		0.00	167.94	19.51	0	10	0	11
C_0_0_60		0.00	311.54	17.17	0	14	0	11
C_1_1_15		632.50	193.70	5.44	0	12	0	11
C_1_1_30		0.00	65.73	5.39	0	7	0	11
C_1_1_45		0.00	25.46	9.74	0	5	1	11
C_1_1_60		0.00	25.46	9.74	0	5	1	11
C_10_10_15		632.50	71.41	0.79	0	9	3	10
C_10_10_30		18.26	60.27	1.39	0	6	2	10
C_10_10_45		18.25	25.46	4.53	0	5	2	10
C_10_10_60		18.25	25.46	4.53	0	5	2	10
C_100_100_15		2755.59	1.38	0.00	0	7	8	14
C_100_100_30		1018.57	0.00	0.00	0	4	5	12
C_100_100_45		553.19	0.00	4.53	0	4	3	12
C_100_100_60		18.27	0.00	4.53	0	4	2	13

[a] C — Campania; λ_1 — minimum productivity penalty; λ_2 — maximum collection capacity penalty; β — accessibility threshold.

while the *BSC-MFLP-CB* provides solutions ranging from 12 open BFs (4 BCs and 8 BSs, for $\alpha = 0.04$) to 14 open BFs (7 BCs and 7 BSs, for $\alpha = 0.06$). Concerning the *BSC-MFLP-SB*$_{max}$ formulation, the number of open BFs align closely with those obtained from the *BSC-MFLP-SB*$_{sum}$ formulation and in most of the cases it is lower than or equal to $BF - CB_{high}$. Thus, the same discussion provided for the *BSC-MFLP-SB*$_{sum}$ holds, with the only exception of the instances with $\beta = 15$. Indeed, for these instances, the number of BFs returned by the *BSC-MFLP-SB*$_{sum}$ is at most 2 units higher w.r.t. $BF - CB_{low}$ and 2 units lower w.r.t. $BF - CB_{high}$. Instead, the number of BFs returned by the *BSC-MFLP-SB*$_{max}$ is at most 8 units higher w.r.t. $BF - CB_{low}$ and 2 units lower w.r.t. $BF - CB_{high}$. Thus, we observe that the *BSC-MFLP-SB*$_{max}$ is more sensitive to the accessibility parameter β w.t.r. the *BSC-MFLP-SB*$_{sum}$ and it returns more conservative solutions in terms of open BFs. Hence, decision-makers should consider this issue and choose the solution coherently with their aversion to risk.

5.3. Experimental results for Apulia region

In this section, we present the results obtained for the Apulia region. In what follows, we start by focusing on the experiments performed for the case-based model (*BSC-MFLP-CB*) — Section 5.3.1. Afterwards, we present those obtained with the scenario-based formulations (*BSC-MFLP-SB*) in Section 5.3.2. In both cases, only a centralized strategy is investigated.

Table 4
Results of $BSC\text{-}MFLP\text{-}SB_{sum}$ and $BSC\text{-}MFLP\text{-}SB_{max}$ for Campania region.

Instance (C_λ_1_λ_2_β)[a]	ObjType	Obj	Φ_{tot}	Ψ_{tot}	δ	#BCs	#BSs	Time (s)
C_0_0_15	Sum	0.00	293.92	60.91	0	12	0	205
C_0_0_30		0.00	348.11	1.66	0	14	0	223
C_0_0_45		0.00	472.70	1.66	0	18	0	220
C_0_0_60		0.00	293.06	5.99	0	13	0	191
C_1_1_15		21.89	171.64	2.77	0	10	0	878
C_1_1_30		5.74	42.91	3.81	0	6	0	2504
C_1_1_45		0.00	14.88	3.55	0	5	0	1345
C_1_1_60		0.00	14.88	3.55	0	5	0	1799
C_10_10_15		550.44	56.46	7.87	0	6	4	7438
C_10_10_30		91.88	27.41	0.81	0	5	2	3684
C_10_10_45		30.17	3.66	3.42	0	4	1	2134
C_10_10_60		30.17	3.66	3.42	0	4	1	2624
C_100_100_15		2658.40	0.45	0.00	0	5	8	57 127
C_100_100_30		713.66	0.00	0.00	0	4	4	13 224
C_100_100_45		129.96	0.00	1.51	0	3	2	3822
C_100_100_60		167.87	0.00	0.00	0	3	2	3460
C_0_0_15	Max	50.89	584.59	4.99	0	22	0	293
C_0_0_30		0.00	601.38	0.00	0	20	0	394
C_0_0_45		0.00	302.59	45.07	0	11	0	276
C_0_0_60		0.00	368.25	0.00	0	14	0	334
C_1_1_15		67.33	360.79	0.00	0	14	1	648
C_1_1_30		4.59	66.67	0.00	0	6	0	4731
C_1_1_45		0.00	36.64	0.00	0	5	0	2734
C_1_1_60		0.00	36.64	0.00	0	5	0	2220
C_10_10_15		923.71	153.22	0.00	0	9	7	1471
C_10_10_30		73.14	44.45	0.00	0	5	2	5046
C_10_10_45		76.31	10.00	0.00	0	4	1	2633
C_10_10_60		76.31	10.00	0.00	0	4	1	2547
C_100_100_15		2719.40	31.72	0.00	0	6	14	1849
C_100_100_30		1071.01	0.03	0.00	0	4	4	271 019
C_100_100_45		315.14	0.00	0.00	0	4	1	4916
C_100_100_60		240.37	0.00	0.00	0	3	2	3281

[a] *C* — Campania; λ_1 — minimum productivity penalty; λ_2 — maximum collection capacity penalty; β — accessibility threshold.

5.3.1. Results of *BSC-MFLP-CB*

The detailed results are displayed in Table 5. Of course, the interpretation of such results follows that presented for the Campania region (see Section 5.2.1). However, it is interesting to note that, differently from the previous case, for the Apulia region, considering the donation rate of the "as-is situation"(α = 0.05), the number of open BFs is not highly affected by the increase of the penalty values and of the accessibility threshold. Indeed, the overall number remains close to 21, but we can observe the downgrade of several existing BCs to BSs. At the same time, we can also note that all the solutions are characterized by quite large Φ_{tot} values, due to fact that most of the BFs do not satisfy the productivity requirement imposed by the decree. Significant reductions of the number of BFs are achievable just in the case of $\alpha = 0.06$ and high values of the average accessibility threshold.

In order to understand this fact, we look into two detailed solutions, i.e., those obtained for the P_100_100_15 and P_100_100_45 instances, displayed in Figs. 5(a) and 5(b), respectively. The former, which is obtained with an accessibility threshold $\beta = 15$ km (the "as-is" one), is characterized by the presence of 20 BFs (5 BCs and 15 BSs), spread throughout the regional territory. This number reduced to 11 BFs (4 BCs and 7 BSs), for β = 45 km. Note that, also in this case, the located facilities are well distributed in the region.

Such results allow us to make the following considerations. First, the elongated shape of the Apulia, the more sparse distribution of the centroids of the municipalities (used, we recall, as representative points where donors' are located) and the more homogeneous distribution of the population among the cities allows to have more distributed solutions in terms of BFs. Second, in most cases, the obtained solutions are not significantly different with respect to the "as-is" configuration for $\alpha = 0.04, 0.05$. This is due to the fact that, considering the number of donors, the Apulia region has a low margin with respect to the self-sufficiency requirement. Thus, relevant savings in terms of located BFs could be obtained only by increasing the number of donors, which is testified by the results obtained for $\alpha = 0.06$.

5.3.2. Results of *BSC-MFLP-SB*

The results for the scenario-based formulations, i.e., $BSC\text{-}MFLP\text{-}SB_{sum}$ and $BSC\text{-}MFLP\text{-}SB_{max}$ are in Table 6. Also in this case, we focus only on the differentiating aspects between the two variants of the *BSC-MFLP-SB* and between the case-based and scenario-based solutions.

Concerning the two variants of the *BSC-MFLP-SB*, we can observe that, regardless of the parameters' setting, they return very similar solutions in terms of both number and type of BFs, and objective function components. This is mainly due to the fact that, in the scenario with $\alpha = 0.04$, the number of donations does not meet the regional demand requirement. This occurrence, together

Table 5
Results of the *BSC-MFLP-CB* for Apulia region.

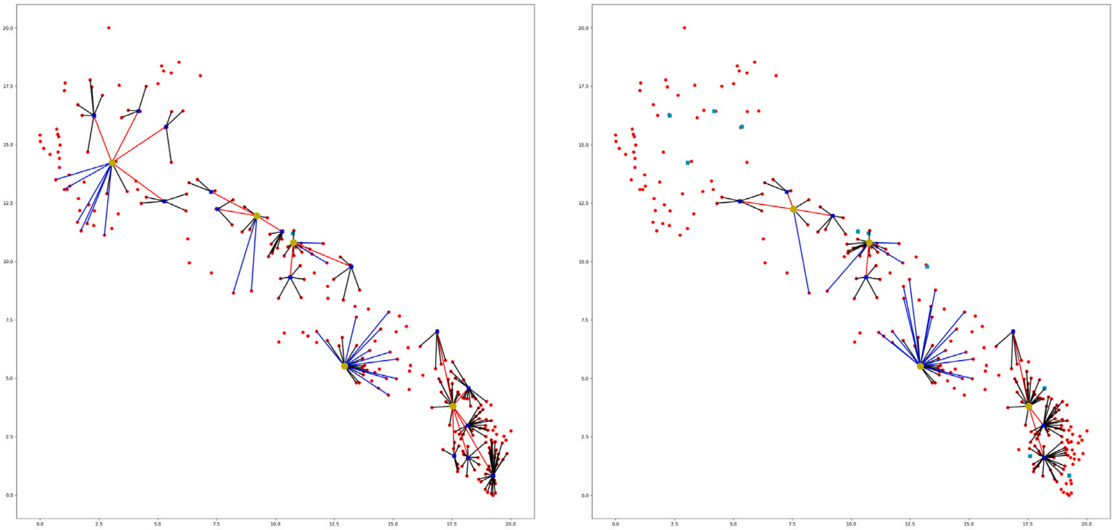
Instance (P_λ_1_λ_2_β)[a]	α	Obj	Φ_{tot}	Ψ_{tot}	δ	#BCs	#BSs	Time (s)
P_0_0_15	0.04	54.96	695.45	0	5.44	21	0	7
P_0_0_30		52.67	652.44	0	2.43	20	0	7
P_0_0_45		52.67	652.44	0	2.43	20	0	7
P_0_0_60		52.67	652.44	0	2.43	20	0	7
P_1_1_15		59.21	615.44	0	5.44	19	2	7
P_1_1_30		58.34	612.43	0	2.43	19	1	8
P_1_1_45		58.34	612.43	0	2.43	19	1	8
P_1_1_60		58.34	612.43	0	2.43	19	1	8
P_10_10_15		2237.98	175.44	0	5.44	8	13	8
P_10_10_30		2037.98	132.43	0	2.43	7	14	8
P_10_10_45		2139.18	172.43	0	2.43	8	13	8
P_10_10_60		2009.92	132.43	0	2.43	7	13	8
P_100_100_15		2237.98	135.44	0	5.44	7	14	9
P_100_100_30		2009.92	132.43	0	2.43	7	13	8
P_100_100_45		1992.89	132.43	0	2.43	7	12	9
P_100_100_60		1992.89	132.43	0	2.43	7	12	9
P_0_0_15	0.05	34.16	682.25	0	0.00	21	0	7
P_0_0_30		0.00	565.89	0	0.00	18	0	7
P_0_0_45		0.00	605.48	0	0.00	19	0	7
P_0_0_60		0.00	565.89	0	0.00	18	0	7
P_1_1_15		54.96	524.42	0	0.00	17	0	9
P_1_1_30		16.73	410.00	0	0.00	14	0	9
P_1_1_45		16.73	410.00	0	0.00	14	0	10
P_1_1_60		16.73	410.00	0	0.00	14	0	9
P_10_10_15		2237.98	86.43	0	0.00	6	13	11
P_10_10_30		1767.95	49.99	0	0.00	5	7	13
P_10_10_45		1767.95	49.99	0	0.00	5	7	13
P_10_10_60		1767.95	49.99	0	0.00	5	7	13
P_100_100_15		3751.91	27.51	0	0.00	5	15	11
P_100_100_30		2535.38	8.57	0	0.00	4	7	14
P_100_100_45		2535.38	8.57	0	0.00	4	7	15
P_100_100_60		2535.38	8.57	0	0.00	4	7	14
P_0_0_15	0.06	40.99	650.70	0	0.00	21	0	7
P_0_0_30		0.00	444.32	0	0.00	15	0	7
P_0_0_45		0.00	444.32	0	0.00	15	0	7
P_0_0_60		0.00	404.32	0	0.00	14	0	7
P_1_1_15		65.95	493.30	0	0.00	17	0	9
P_1_1_30		2.23	210.00	0	0.00	9	0	10
P_1_1_45		2.23	210.00	0	0.00	9	0	10
P_1_1_60		2.23	210.00	0	0.00	9	0	10
P_10_10_15		1741.36	147.20	0	0.00	8	10	11
P_10_10_30		986.45	50.58	0	0.00	5	2	15
P_10_10_45		986.45	50.58	0	0.00	5	2	14
P_10_10_60		986.45	50.58	0	0.00	5	2	15
P_100_100_15		4240.39	11.23	0	0.00	5	15	11
P_100_100_30		2020.21	0.05	0	0.00	4	6	23
P_100_100_45		2020.21	0.05	0	0.00	4	6	19
P_100_100_60		2020.21	0.05	0	0.00	4	6	19

[a] *P* — Apulia; λ_1 — minimum productivity penalty; λ_2 — maximum collection capacity penalty; β — accessibility threshold.

with the very high value imposed for λ_3, hijacks the solution, keeping open all the existing BFs in order to collect the maximum amount of donations. The comparison of the *BSC-MFLP-SB* with *BSC-MFLP-CB* suffers from the same drawback. This is confirmed by the fact that the solutions of the *BSC-MFLP-SB* are very similar to those the *BSC-MFLP-CB* with $\alpha = 0.04$. Thus, the performed experimentation highlights that Apulia region is much more sensitive to blood donation fluctuations.

5.4. Experimental results for Lombardy region

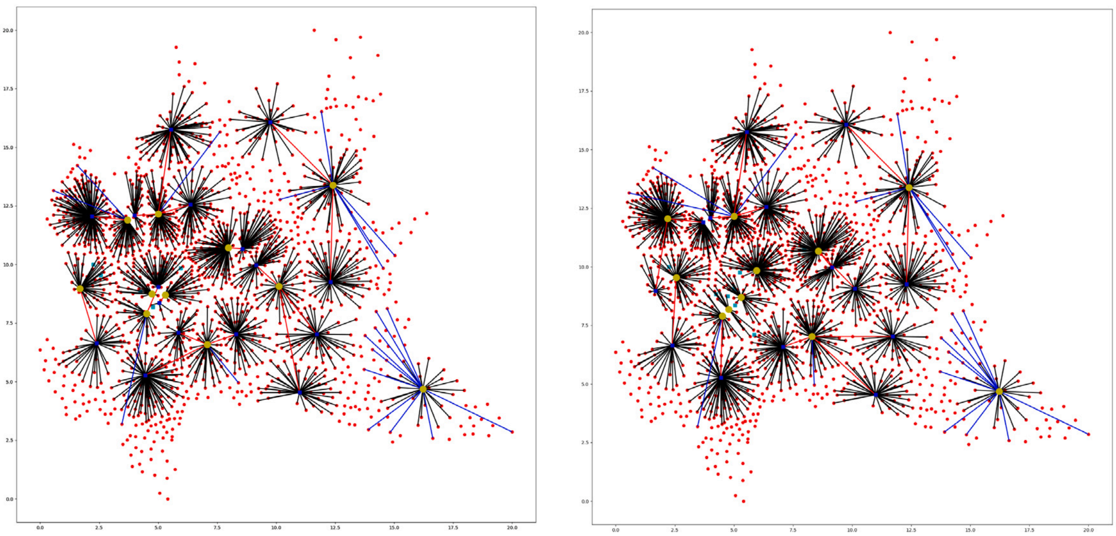
The last step of our empirical analysis consists of additional experiments performed on Lombardy, the largest Italian region. Following the above adopted scheme, we split the results in two parts: Section 5.4.1, containing the results of the *BSC-MFLP-CB* with the centralized strategy; Section 5.4.2, concerning the results of the *BSC-MFLP-SB* variants.



(a) P_100_100_15 solution

(b) P_100_100_45 solution

Fig. 4. Comparison of *BSC-MFLP-CB* solutions for Lombardy region ($\alpha = 0.05$)



(a) L_100_100_15 solution

(b) L_100_100_45 solution

Fig. 5. Comparison of *BSC-MFLP-CB* solutions for Apulia instances ($\alpha = 0.05$)

Table 6
Results of *BSC-MFLP-SB*$_{sum}$ and *BSC-MFLP-SB*$_{max}$ for Apulia region.

Instance (P_λ_1_λ_2_β)[a]	ObjType	Obj	Φ_{tot}	Ψ_{tot}	δ	#BCs	#BSs	Time (s)
P_0_0_15	Sum	190.00	676.14	0	1.81	21	0	34
P_0_0_30		186.00	635.30	0	0.81	20	0	33
P_0_0_45		172.00	635.73	0	0.81	20	0	33
P_0_0_60		172.00	635.73	0	0.81	20	0	34
P_1_1_15		262.35	596.13	0	1.81	19	2	43
P_1_1_30		209.45	595.72	0	0.81	19	1	42
P_1_1_45		209.45	595.72	0	0.81	19	1	43
P_1_1_60		209.45	595.72	0	0.81	19	1	41
P_10_10_15		1779.94	198.03	0	1.81	9	12	52
P_10_10_30		2231.86	119.53	0	0.81	7	13	51
P_10_10_45		2231.86	119.53	0	0.81	7	13	52
P_10_10_60		2231.86	119.53	0	0.81	7	13	48
P_100_100_15		3464.85	107.11	0	1.81	7	14	46
P_100_100_30		3164.63	95.60	0	0.81	7	13	50
P_100_100_45		3164.63	95.60	0	0.81	7	13	53
P_100_100_60		3164.63	95.60	0	0.81	7	13	48
P_0_0_15	Max	636.57	695.45	0	5.44	21	0	37
P_0_0_30		689.64	652.44	0	2.43	20	0	32
P_0_0_45		689.64	612.44	0	2.43	19	0	32
P_0_0_60		689.64	652.44	0	2.43	20	0	31
P_1_1_15		698.07	615.44	0	5.44	19	2	49
P_1_1_30		719.69	612.43	0	2.43	19	1	45
P_1_1_45		691.19	612.43	0	2.43	19	0	44
P_1_1_60		691.19	612.43	0	2.43	19	0	43
P_10_10_15		1937.67	215.44	0	5.44	9	12	50
P_10_10_30		2161.01	172.43	0	2.43	8	13	48
P_10_10_45		2131.95	172.43	0	2.43	8	12	47
P_10_10_60		2161.01	172.43	0	2.43	8	13	50
P_100_100_15		2766.05	135.44	0	5.44	7	14	50
P_100_100_30		2454.30	132.43	0	2.43	7	13	57
P_100_100_45		2454.30	132.43	0	2.43	7	13	56
P_100_100_60		2454.30	132.43	0	2.43	7	13	54

[a] *P* — Apulia; λ_1 — minimum productivity penalty; λ_2 — maximum collection capacity penalty; β — accessibility threshold.

5.4.1. Results of BSC-MFLP-CB

The results obtained for these experiments are reported in Table 7. As for the Campania and Apulia regions, similar patterns are again observed concerning productivity and capacity restrictions, on the one hand, and with accessibility, on the other.

Therefore, here we only focus on an (novel) aspect of great relevance emerging from the results, which shed light on the proper functioning of the regional BSC. Lombardy, we recall, is the largest region in Italy in terms of population, and the region where most medical treatments are conducted as people migrate from all over Italy to seek care. However, Lombardy only manages to meet the self-sufficiency goal when the value of α equals 0.06 (note the non-zero values for δ in the Table). We want to emphasize that the assumed data of 5 donations per 1000 inhabitants is an aggregate figure for Italy, and the specific reference value for Lombardy is actually higher. Nevertheless, we highlight the importance of implementing policies aimed at maintaining this value to ensure the smooth operation of the system. Indeed, if the donation rate was to fall below the threshold of 6 donations per 1000 inhabitants, the region could face difficulties in sourcing the necessary blood for self-sufficiency, making it essential to purchase blood units from other Italian regions.

Figs. 4(a) and 4(b), representing the solutions obtained for the L_100_100_15 and L_100_100_45 instances (for $\alpha = 0.05$), give an insight into this situation. The solution obtained for L_100_100_15 solution utilizes a total of 26 BFs (comprising 11 BCs and 15 BSs) strategically scattered across the regional territory. Alternatively, by raising the accessibility threshold to 45 km, the L_100_100_45 solution achieves similar results with only 1 BSs less. This demonstrates that, despite increasing the accessibility threshold, the solution remains relatively unchanged due to the inability to meet the entire regional demand for blood.

5.4.2. Results of BSC-MFLP-SB

Table 8 present the results for two variations of the centralized strategy: *BSC-MFLP-SB*$_{sum}$ and *BSC-MFLP-MS*$_{max}$. When considering the two variants of *BSC-MFLP-SB*, we observe that regardless of the parameter settings, they produce very similar solutions in terms of both the number and type of blood facilities (BFs). This similarity is primarily attributed to the fact that, in scenarios with $\alpha = 0.04$ and $\alpha = 0.05$, the number of donations fails to meet the regional demand for blood (self-sufficiency). To maximize the amount of collected donations, the model tends to keep all existing BFs open due to the high value assigned to λ_3.

Table 7
Results of *BSC-MFLP-CB* for Lombardy region.

Instance (L_λ_1_λ_2_β)[a]	α	Obj	Φ_{tot}	Ψ_{tot}	δ	#BCs	#BSs	Time (s)
L_0_0_15	0.04	320.00	624.94	18.15	101.16	24	0	583
L_0_0_30		320.00	607.85	6.68	101.16	24	0	537
L_0_0_45		320.00	608.03	6.04	101.16	24	0	538
L_0_0_60		320.00	608.03	6.04	101.16	24	0	571
L_1_1_15		320.00	631.16	0.00	101.16	25	0	1851
L_1_1_30		320.00	631.16	0.00	101.16	25	0	1738
L_1_1_45		320.00	631.16	0.00	101.16	25	0	1764
L_1_1_60		320.00	631.16	0.00	101.16	25	0	1761
L_10_10_15		2168.86	315.11	0.00	101.16	17	14	2021
L_10_10_30		2168.86	315.11	0.00	101.16	17	14	2011
L_10_10_45		2177.66	314.23	0.00	101.16	17	12	2049
L_10_10_60		1582.73	273.73	0.00	101.16	16	11	2038
L_100_100_15		4204.30	111.16	0.00	101.16	12	17	2056
L_100_100_30		7825.90	81.27	0.00	101.16	9	20	2158
L_100_100_45		7193.40	64.94	0.00	101.16	9	15	2143
L_100_100_60		7193.40	64.94	0.00	101.16	9	15	2064
L_0_0_15	0.05	360.00	667.72	9.01	8.95	26	0	609
L_0_0_30		360.00	601.97	4.40	8.95	26	0	579
L_0_0_45		360.00	593.13	4.17	8.95	26	0	593
L_0_0_60		360.00	517.29	38.34	8.95	26	0	575
L_1_1_15		449.02	530.98	0.00	8.95	25	2	1817
L_1_1_30		363.55	506.45	0.00	8.95	24	0	1884
L_1_1_45		363.55	506.45	0.00	8.95	24	0	1742
L_1_1_60		363.55	506.45	0.00	8.95	24	0	1830
L_10_10_15		2110.60	128.67	40.27	8.95	16	10	2171
L_10_10_30		1685.56	168.51	1.93	8.95	15	7	2194
L_10_10_45		1689.20	169.08	0.00	8.95	15	7	2355
L_10_10_60		1724.19	165.71	4.87	8.95	14	8	2013
L_100_100_15		4517.80	24.42	0.00	8.95	11	15	2247
L_100_100_30		4011.30	24.02	0.00	8.95	11	14	2230
L_100_100_45		4011.30	24.02	0.00	8.95	11	14	2243
L_100_100_60		4011.30	24.02	0.00	8.95	11	14	2440
L_0_0_15	0.06	0.00	670.72	0.00	0.00	30	0	622
L_0_0_30		0.00	472.23	40.53	0.00	23	0	538
L_0_0_45		0.00	455.96	69.47	0.00	22	0	525
L_0_0_60		0.00	383.31	78.97	0.00	19	0	518
L_1_1_15		6.19	226.70	9.75	0.00	17	0	2209
L_1_1_30		0.00	50.23	3.70	0.00	12	0	4229
L_1_1_45		0.00	50.23	3.70	0.00	12	0	4469
L_1_1_60		0.00	50.23	3.70	0.00	12	0	4850
L_10_10_15		618.12	122.04	1.69	0.00	15	3	9104
L_10_10_30		374.43	10.32	1.43	0.00	11	0	7821
L_10_10_45		374.43	10.32	1.43	0.00	11	0	8231
L_10_10_60		374.43	10.32	1.43	0.00	11	0	6175
L_100_100_15		3122.59	0.04	0.00	0.00	12	13	12 659
L_100_100_30		594.23	0.02	0.00	0.00	11	1	13 727
L_100_100_45		594.23	0.02	0.00	0.00	11	1	15 512
L_100_100_60		594.23	0.02	0.00	0.00	11	1	13 305

[a] L — Lombardy; λ_1 — minimum productivity penalty; λ_2 — maximum collection capacity penalty; β — accessibility threshold.

Table 8
Results of $BSC\text{-}MFLP\text{-}SB_{sum}$ and $BSC\text{-}MFLP\text{-}SB_{max}$ for Lombardy region.

Instance (L_λ_1_λ_2_β)[a]	ObjType	Obj	Φ_{tot}	Ψ_{tot}	δ	#BCs	#BSs	Time (s)
L_0_0_15	Sum	219.89	573.33	53.25	29.76	24	0	3070
L_0_0_30		219.89	608.87	7.08	29.76	26	0	3048
L_0_0_45		219.89	515.81	31.81	29.76	23	0	3061
L_0_0_60		219.89	664.91	0.00	29.76	28	0	3326
L_1_1_15		551.24	591.87	0.00	29.76	26	3	11 729
L_1_1_30		551.24	587.83	0.00	29.76	26	3	12 860
L_1_1_45		431.78	626.89	0.00	29.76	23	3	13 299
L_1_1_60		229.23	442.78	85.00	29.76	20	0	11 907
L_10_10_15		1883.75	352.03	0.00	29.76	20	11	17 088
L_10_10_30		1989.92	347.56	0.00	29.76	19	13	13 401
L_10_10_45		1989.92	318.95	0.00	29.76	19	13	14 124
L_10_10_60		1746.23	309.55	0.00	29.76	13	9	15 549
L_100_100_15		2574.01	50.64	4.36	29.76	12	13	19 122
L_100_100_30		2997.43	38.66	0.00	29.76	10	16	18 490
L_100_100_45		3012.99	35.06	0.00	29.76	10	16	18 918
L_100_100_60		3231.88	30.11	4.90	29.76	9	14	17 425
L_0_0_15	Max	287.43	639.32	0.00	101.16	25	0	3104
L_0_0_30		287.43	660.87	59.70	101.16	24	0	2907
L_0_0_45		287.43	648.29	7.12	101.16	25	0	3215
L_0_0_60		287.43	578.06	16.89	101.16	23	0	2955
L_1_1_15		688.11	711.16	0.00	101.16	27	3	12 298
L_1_1_30		688.11	671.16	0.00	101.16	26	3	12 860
L_1_1_45		716.29	591.16	0.00	101.16	23	4	13 299
L_1_1_60		287.43	551.16	0.00	101.16	23	0	12 208
L_10_10_15		1975.67	432.19	0.00	101.16	20	13	13 950
L_10_10_30		2030.96	391.16	0.00	101.16	19	13	12 816
L_10_10_45		2030.96	391.16	0.00	101.16	19	13	14 916
L_10_10_60		1696.06	198.37	33.60	101.16	13	9	15 710
L_100_100_15		2966.70	111.80	0.00	101.16	12	12	19 130
L_100_100_30		3915.52	86.13	0.00	101.16	11	14	20 462
L_100_100_45		3892.48	74.97	0.00	101.16	11	14	19 091
L_100_100_60		5306.65	35.85	0.00	101.16	9	14	22 184

[a] L — Lombardy; λ_1 — minimum productivity penalty; λ_2 — maximum collection capacity penalty; β — accessibility threshold.

A similar observation holds when focusing on the comparison between *BSC-MFLP-SB* and *BSC-MFLP-CB*. The solutions generated by *BSC-MFLP-SB* closely resemble those of *BSC-MFLP-CB* when α is set equal to 0.05. This further demonstrates that the Lombardy region, like Apulia, is highly susceptible to fluctuations in blood donations, necessitating the maintenance of a sufficiently high donation rate to address this issue. In contrast, Campania is less affected by these variations.

6. Conclusions

This work investigates the reorganization of regional blood management systems from a strategic perspective. It is directed forward the closing or reconverting of blood facilities currently operating in a region, finding good trade-off solutions between the need of attracting donors (self-sufficiency objective) and the need of reducing the system management costs (efficiency objective). To this aim, we proposed two MILP formulations tackling a multi-echelon facility location problem in a case-based and scenario-based perspective.

The proposed formulations allow, on the one hand, to provide insights on the impact of several strategies and policies in the reorganization of the regional BSC and, on the other, to perform a sensitivity of the proposed solutions to the variation of several parameters and different scenarios. Thus, it can represent a useful decision support system for the competent authorities and stakeholders.

The model has been validated on three real cases related to the Campania, Apulia and Lombardy regions, for which several configurations have been simulated. The experimentation has allowed to derive several suggestions for an effective reorganization of the "as-is" situations in the regions under investigation and has highlighted the importance of taking into account the specific demographic and topological features of a territory, as well as the structural deficiencies of the system.

Future research directions naturally include the integration of tactical and operational issues, such as workforce planning and mobile unit routing. As a consequence, the need of developing either heuristic and meta-heuristic solution methods or advanced multi-stage stochastic programming approaches could arise. Moreover, we recall that our methodology is specifically designed to address the requirements of a European Directive, which encompasses not only Italy but also other countries. As a result, we believe that our proposed modeling framework holds relevance for other countries that are currently undergoing or considering a reorganization of their BSC. Therefore, future work perspective will include the adaptation of our modeling framework to different national contexts, incorporating and tailoring different BSC peculiarities.

CRediT authorship contribution statement

Antonio Diglio: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Validation, Writing – original draft, Writing – review & editing. **Andrea Mancuso:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Validation, Writing – original draft, Writing – review & editing. **Adriano Masone:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Validation, Writing – original draft, Writing – review & editing. **Claudio Sterle:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Validation, Writing – original draft, Writing – review & editing.

Acknowledgments

Research presented in the paper has been partially funded by the National Centre for Sustainable Mobility "CN MOST" (MUR code CN00000023 - CUP UNINA code: E63C22000930007) and by the MUR research program, PRIN 2022 founded by European Union – Next Generation EU (Project "ACHILLES, eco-sustAinable effiCient tecH-drIven Last miLE logiStics", Prot. 2022BC2CW7, CUP: E53D23005630006).

Appendix A. Supplementary data

Supplementary material related to this article can be found online at https://doi.org/10.1016/j.tre.2024.103438.

References

Ahmadi-Javid, A., Seyedi, P., Syam, S.S., 2017. A survey of healthcare facility location. Comput. Oper. Res. 79, 223–263.
Arani, M., Chan, Y., Liu, X., Momenitabar, M., 2021. A lateral resupply blood supply chain network design under uncertainties. Appl. Math. Model. 93, 165–187.
Attari, M.Y.N., Pasandideh, S.H.R., Aghaie, A., Niaki, S.T.A., 2018. A bi-objective robust optimization model for a blood collection and testing problem: an accelerated stochastic benders decomposition. Ann. Oper. Res. 1–39.
AVIS, 2021. Il sistema trasfusionale campano e la raccolta associativa. https://www.avis.it/wp-content/uploads/attachments/4305_documento.pdf.
Beliën, J., Forcé, H., 2012. Supply chain management of blood products: A literature review. European J. Oper. Res. 217 (1), 1–16.
Bruno, G., Diglio, A., Piccolo, C., Cannavacciuolo, L., 2019. Territorial reorganization of regional blood management systems: Evidences from an Italian case study. Omega 89, 54–70.
Catalano, L., Piccinini, V., Pati, I., Masiello, F.G., Marano, G., Pupella, S., De Angelis, V., 2021. Italian Blood System 2020: Activity Data, Haemovigilance and Epidemiological Surveillance. Rapporti ISTISAN 21/14.
Cetin, E., Sarul, L.S., 2009. A blood bank location model: A multiobjective approach. Eur. J. Pure Appl. Math. 2 (1), 112–124.
Chaiwuttisak, P., Smith, H., Wu, Y., Potts, C., Sakuldamrongpanich, T., Pathomsiri, S., 2016. Location of low-cost blood collection and distribution centres in thailand. Oper. Res. Health Care 9, 7–15.
Correia, I., Saldanha-da Gama, F., 2019. Facility location under uncertainty. Locat. Sci. 185–213.
Diglio, A., Mancuso, A., Masone, A., Piccolo, C., Sterle, C., 2021. A MILP formulation for the reorganization of the blood supply chain in Italian regions. In: Optimization and Data Science: Trends and Applications. In: AIRO Springer Series, In: AIRO Springer Series, vol. 6.51–66,
Elalouf, A., Hovav, S., Tsadikovich, D., Yedidsion, L., 2015. Minimizing operational costs by restructuring the blood sample collection chain. Oper. Res. Health Care 7, 81–93.
Gazzetta Ufficiale, 2013. Linee guida per l'accreditamento dei servizi trasfusionali e delle unità di raccolta del sangue e degli emocomponenti (allegato A). https://www.gazzettaufficiale.it/atto/serie_generale/caricaArticolo?art.progressivo=0&art.idArticolo=1&art.versione=1&art.codiceRedazionale=13A03965&art.dataPubblicazioneGazzetta=2013-05-09&art.idGruppo=0&art.idSottoArticolo1=10&art.idSottoArticolo=1&art.flagTipoArticolo=1.
Govindan, K., Fattahi, M., Keyvanshokooh, E., 2017. Supply chain network design under uncertainty: A comprehensive review and future research directions. European J. Oper. Res. 263 (1), 108–141.
Hamdan, B., Diabat, A., 2019. A two-stage multi-echelon stochastic blood supply chain problem. Comput. Oper. Res. 101, 130–143.
ISTAT, 2011. Dati del censimento generale della popolazione Italiana (Italian national census data). URL: www.istat.it [accessed on July 21, 2022].
Jabbarzadeh, A., Fahimnia, B., Seuring, S., 2014. Dynamic supply chain network design for the supply of blood in disasters: A robust model with real world application. Transp. Res. E 70, 225–244.
Laporte, G., Nickel, S., da Gama, F.S., 2019. Location Science, vol. 528, Springer.
Liu, W., Ke, G.Y., Chen, J., Zhang, L., 2020. Scheduling the distribution of blood products: A vendor-managed inventory routing approach. Transp. Res. E 140, 101964.
Meneses, M., Santos, D., Barbosa-Póvoa, A., 2022. Modelling the blood supply chain–from strategic to tactical decisions. European J. Oper. Res..
Ministero della Salute, 2021. Servizi trasfusionali. https://www.salute.gov.it/portale/temi/p2_6.jsp?lingua=italiano&id=2949&area=sangueTrasfusioni&menu=trasfusionale.
Momenitabar, M., Dehdari Ebrahimi, Z., Arani, M., Mattson, J., 2022. Robust possibilistic programming to design a closed-loop blood supply chain network considering service-level maximization and lateral resupply. Ann. Oper. Res. 1–43.
Moslemi, S., Pasandideh, S.H.R., 2021. A location-allocation model for quality-based blood supply chain under IER uncertainty. RAIRO-Oper. Res. 55, S967–S998.
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. Int. J. Prod. Res. 53 (24), 7191–7212.
Osorio, A.F., Brailsford, S.C., Smith, H.K., 2018. Whole blood or apheresis donations? A multi-objective stochastic optimization approach. European J. Oper. Res. 266 (1), 193–204.
Pirabán, A., Guerrero, W.J., Labadie, N., 2019. Survey on blood supply chain management: Models and methods. Comput. Oper. Res. 112, 104756.
Rais, A., Viana, A., 2011. Operations research in healthcare: a survey. Int. Trans. Oper. Res. 18 (1), 1–31.
Rameshwar, D., Angappa, G., Thanos, P., 2019. Application of Operations Research (OR) in Disaster Relief Operations (DRO), Part I and Part II. 283, (1-2), Bantam,
Ramezanian, R., Behboodi, Z., 2017. Blood supply chain network design under uncertainties in supply and demand considering social aspects. Transp. Res. E 104, 69–82.
Şahin, G., Süral, H., Meral, S., 2007. Locational analysis for regionalization of turkish red crescent blood services. Comput. Oper. Res. 34 (3), 692–704.

Samani, M.R.G., Hosseini-Motlagh, S.-M., Ghannadpour, S.F., 2019. A multilateral perspective towards blood network design in an uncertain environment: Methodology and implementation. Comput. Ind. Eng. 130, 450–471.
Tirkolaee, E.B., Golpîra, H., Javanmardan, A., Maihami, R., 2023. A socio-economic optimization model for blood supply chain network design during the COVID-19 pandemic: An interactive possibilistic programming approach for a real case study. Soc.-Econ. Plan. Sci. 85, 101439.
World Health Organization, 2021. 10 Facts on blood transfusion. https://www.who.int/bloodsafety/FactFile2009.pdf.
World Health Organization, et al., 2017. Regional Status Report on Blood Safety and Availability 2016. Technical Report, World Health Organization. Regional Office for the Eastern Mediterranean.
Zahiri, B., Pishvaee, M.S., 2017. Blood supply chain network design considering blood group compatibility under uncertainty. Int. J. Prod. Res. 55 (7), 2013–2033.
Zahiri, B., Torabi, S., Mousazadeh, M., Mansouri, S., 2015. Blood collection management: Methodology and application. Appl. Math. Model. 39 (23–24), 7680–7696.