Optimizing Vaccine Supply Chain in Rural Areas: Insights from a Mountainous Italian Province

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Abstract: The pandemic has brought the logistics of vaccine distribution to the forefront of discussions in the healthcare sector. However, it is important to recognise that an efficient vaccine supply chain is crucial not only in emergencies but also for regularly distributed and administered vaccines. This paper presents a case study on the influenza vaccine supply chain in a mountainous Italian province. The location of vaccine hubs can significantly impact access to vaccines for vulnerable patients. The case study compares the current location of these hubs with theoretically optimal locations identified through facility location problem algorithms. Moreover, it examines how collaboration between health authorities can improve vaccine distribution routes through vehicle routing problem algorithms. By collaborating, health authorities can establish a strong foundation for a national distribution pathway that can be activated in times of crisis. This work applies well-established models to a real-world case, providing valuable insights into the practical application of these concepts. The results of this case study could have important implications for improving access to vaccines and ensuring that vulnerable populations living in rural areas receive the care they need.

Keywords: facility location problem; vehicle routing problem; vaccine; supply chain.

I. INTRODUCTION

In the healthcare sector, the appropriate choice of where to locate medical facilities and the correct schedule of goods delivery are essential for providing effective care; an example is vaccine distribution. Vaccine logistics (i.e., the set of activities allowing receiving, storing, and transporting vaccines at proper temperatures and promptly getting them to the right places [1]) has become one of the most crucial topics discussed in the healthcare sector. The interest in the logistic aspect of vaccine distribution should not be a priority only in "black swan" situations like a pandemic: having an efficient and strong vaccine supply chain for the distribution and administration of regularly used vaccines can be an important base for the development of a national and/or international distribution pathway in emergency circumstances. If not well managed, the location of the hubs and the distribution of vaccines can result in poor access to immunisations and restricted adherence to the vaccination campaign, with potentially negative sequelae for people's health [2]. This issue occurs especially for vulnerable citizens, i.e., people with chronic or acute illnesses that could increase the risk of complications in the event of infection. Frail individuals experience more difficulties reaching vaccination hubs, especially if they require a caregiver's assistance and live in mountainous or isolated areas. This paper focuses on the analysis of the influenza vaccine supply chain in the district of Bergamo, a province in northern Italy, whose surface is largely occupied by mountainous areas. The case study is examined from the perspective of frail people. The objective is to compare alternative networks built using facility location theoretical models, like the *p*-median and *p*-center, with the current situation as it is. In addition, the paper will compare the as-is situation of the distribution of vaccines in the province with the theoretically optimal one identified through the Vehicle Routing Problem (VRP). In relation to this last point, mention will be made of the concept of shared resources and horizontal collaboration among the three health authorities in charge of distributing and administering vaccines to the territory's population. Even if such topics are quite common in managerial literature, the originality of this work is related to the practical application of well-established models to a real-world case. The manuscript is subdivided in theoretical background (Section 2), methodology (Section 3), as-is situation and results (Section 4), discussion (Section 5), and conclusions with future work.

II. BACKGROUND

The problem of locating facilities and managing goods distribution covers the core topics of distribution system design [3]. Most of the literature concerning the design of a vaccine network relates to the pandemic response. The SARS-CoV-2 pandemic severely impacted the global healthcare supply chain. As a result, healthcare managers must devise a strategy to improve their healthcare supply networks. Applying operations research techniques offers a chance to enhance the healthcare industry [4]. The most discussed topic regarding the vaccine supply chain is the location of the dispensing sites. Much of the literature regarding facility location in the context of vaccination networks focuses on the siting of vaccination centres in reaction to a pandemic and/or epidemic [5] or to vaccinate children in underdeveloped nations [6]. The location of vaccine centres is equally important when designing a vaccine network in rural or mountainous areas. In mountainous and/or rural areas, the criticality of facility location is worsened: people living in such areas face considerable burdens in travel time to healthcare services [7]. Once the vaccinal network has been identified, the vaccine doses should be transported from the warehouses to the point of dispensing. Some researchers describe a general mathematical programming model that can be readily adapted as a planning tool to analyse scenarios relevant to a vaccine supply chain [8]. Most papers concern vaccine distribution in low- and middle-income countries for children's vaccination. For instance, some researchers provide a mathematical model for redesigning the World Health Organization's Expanded Program on Immunization vaccine distribution network [9]. From sustainable transportation and logistics perspective, collaboration is key to improving travel efficiency, reducing operational costs, and achieving sustainable development [10]. Two types of collaborations exist, namely, vertical collaborations, which are performed by the actors of a logistics network at different levels, and horizontal collaborations, which are operated by the participants of a logistics network at the same level. Horizontal collaboration is a promising supply chain management strategy to reduce transportation and logistics costs while increasing customer service levels. A collaborative transportation system can be defined as two or more carriers that follow a collaborative transportation pooling approach by sharing material and immaterial resources [11]. Researchers [12] have studied the role of collaborative transport in urban areas, but applications to rural areas are limited. In summary, the literature regarding the vaccine supply chain focuses on two main aspects: the optimal location of hubs and the distribution of vaccine doses within the network. These two macro-topics are often considered separately. Furthermore, to the best of our knowledge, research on the vaccine supply chain in mountainous areas is scarce. In terms of vaccine distribution, horizontal collaboration among transporters in rural regions will be investigated, an area of research that has received little attention. The current paper analyses hubs' location and vaccine distribution simultaneously through the application of optimisation algorithms to the vaccination network for frail individuals in a mountainous Italian province.

III. MATERIALS AND METHODS

A case study, specifically "single-case design," was the methodology selected for this paper. Research by case study was preferred since it enables a more descriptive and exploratory approach, allowing for more rich insights into the research objective[13]. The single case study makes researchers aware of the possible consequences of certain kinds of institutional strategies. For policymakers, the experiences of the case study, and the discussion of the challenges that may be expected when managing a vaccine distribution chain, will help to promote awareness of the main problems. Researchers might select cases that are most likely to exhibit behaviours that they are interested in investigating [14]. For this reason, we decided to analyse the vaccine network of the Italian province of Bergamo, which is characterised by densely populated areas and less populated and more difficult-to-reach mountainous areas. Consequently, comparing as-is and optimisation models results could provide interesting insights into how to make vaccine distribution more widespread. For this purpose, collecting data on the vaccination network was necessary. A semi-structured interview protocol was developed. The director of the territorial pharmaceutical department, responsible for the purchase and distribution of vaccines, and various employees of the vaccination hubs were interviewed. We also collected archival data from the territorial health authority website and reports published by government agencies. The data collected concerned the vaccination network as well as demographic data concerning the territorial distribution of frail patients.

IV. RESULT

In the Bergamo province, frail individuals receive vaccination in one of the sixteen vaccinal hubs managed by the territorial pharmaceutical service (Figure 1). Citizens are assigned to the hubs according to the distance between their municipality of residence and the hubs. The territorial pharmaceutical service, located in the city of Bergamo, plays the roles of the purchaser, central supplier, and storage centre for all the hubs of the province. Additionally, the hubs are grouped into territorial districts; there are a total of seven territorial districts in the province. To ensure comparability between the as-is network and the theoretical network identified through the optimisation models, we decided to keep the number of active vaccination hubs and the division into districts constant. In the current situation, vaccine hubs are almost exclusively located around the city of Bergamo, far from mountainous areas. This solution can make access to the vaccine difficult for frail people living in areas far from the city. Vaccines are stored in the central warehouse, which is also a hub of the territorial pharmaceutical service in Bergamo. From here, the doses are distributed weekly to the hubs according to a predefined schedule requiring four working days (Figure 1). Each hub is visited only once a week. Each of the three territorial health authorities is autonomous in collecting and distributing the doses to their respective hubs; there is no collaboration in distribution between the three health authorities. Therefore, deliveries are made within four working days (one territorial authority travels to all its hubs in two days, while the other two do so in one).

Figure 1. AS-IS vaccinal hub location and doses distribution routes.

A. *Hubs location*

Facility location problems aim to identify the optimal spatial location of one or more facilities of interest to meet customer demand [15]. In the considered case, the facilities to be located correspond to vaccination centres, while the demand to be satisfied coincides with that of fragile residents of the province of Bergamo. We tested several known and consolidated logistical models for the centres' locations, each substantiating slightly different objectives.

Distance minimisation

Among the various criteria that could be adopted for localisation, the first option is to minimise the maximum distance w between any municipality in the province and its closest vaccination hub. The assignment of patients to hubs is done through the municipality of residence. This strategy reflects the current provincial organisation in which citizens are assigned to the vaccine hub based on their municipality of residence. Accordingly, the first implemented model is the *p*-center [16]. Let p be the number of vaccinal hubs that must be opened in the province; $N = 1, \dots, n$ be the set of municipalities of the province in which a vaccinal hub could be opened, $d_i (i \in N)$ be the vaccine demand of each municipality, i.e., the number of frail residents of each municipality, and $dist_{ij}$ the distance between municipalities i and j $(i, j \in N)$. The decision variables are:

$$x_{ij} = \begin{cases} 1 \; iff \; municipality \; i \; is \; assigned \; to \; vaccinal \; hub \; j \\ 0 \quad otherwise \end{cases}$$

$$y_j = \begin{cases} 1 \; iff \; in \; municipality \; j \; a \; vaccinal \; hub \; is \; opened \; 0 \\ 0 \quad otherwise \end{cases}$$

The objective function is:

$$\text{Min } w \tag{1}$$

Subject to:

$$\sum_{j \in N} y_j = p \tag{2}$$

$$\sum_{j \in N} x_{ij} = 1, \;\; \forall i \in N \tag{3}$$

$$x_{ij} \le y_j, \forall i, j \in N \tag{4}$$

$$\sum_{j \in N} dist_{ij} \cdot x_{ij} \le w, \forall i \in N \tag{5}$$

$$x_{ij} \in \{0,1\} \; \forall i, j \in N \; and \; y_j \in \{0,1\} \; \forall j \in N \tag{6}$$

Constraint (2) ensures that exactly the desired number of vaccinal hubs p is opened. Constraint set (3) stipulates that each municipality is assigned to one and only one vaccinal hub. Finally, constraint set (4) ensures that each municipality is assigned to an active vaccinal hub. Constraint (5) is needed to check that w is the maximum distance between municipalities and the opened vaccinal hubs. Constraint set (6) bounds the variables domain. The main problem to which this type of criterion may lead is the proposed activation of a vaccine hub in isolated and small municipalities not equipped with the necessary infrastructure. An emblematic example is the case of the district "Valle Brembana and Imagna". Its vaccination hubs are currently located in the municipalities of Villa d'Almè (hub number 1 in Figure 2) and Zogno (Hub number 2 in Figure 2), municipalities of approximately 6600 and 8600 inhabitants, respectively. Minimising the maximum distance between vaccination hubs and municipalities led to the hubs being located in the municipalities of Ubiale Clanezzo (hub A in Figure 2) and Valnegra (hub B in Figure 2) (of approximately 1400 and 200 inhabitants, respectively). The solution identified would make it possible to simplify the reception of the vaccine for frail residents of the mountainous area, compared to the current organisation whereby the two vaccine hubs are both concentrated in the hinterland of the city of Bergamo. However, Valnegra, being small in size, would be inadequate from an infrastructural point of view to hosting a vaccine hub. The poor feasibility of the theoretical solution obtained is due to the nature of the criterion adopted to guide the solution of the problem, which aimed exclusively at minimising the maximum distance between the municipalities and their closest vaccination hub, regardless of the specific demand of each municipality. This result does not necessarily mean that the distance minimisation criterion is incorrect; it relies on the kind of problem that needs to be solved. Therefore, in a mountainous area where the layout and infrastructure of mountain municipalities differ significantly from that of cities, the p-center model may not be the best option for streamlining the access of frail patients to the vaccination network. One option might be to remove too small municipalities from the selection as hub locations to overcome this limitation. However, it is difficult to understand the right threshold below which the exclusion of cities makes sense. Furthermore, some municipalities may have a low number of inhabitants but, at the same time, have a strategic position or relevance in the mountainous area and are suitable for hosting a hub. An alternative solution is to add the "weight" of each city—that is, the proportion of vulnerable residents—as a location criterion.

Weighted distance minimisation

To overcome the p-center limitation for hub location, the distance between hubs and municipalities must be minimised while accounting

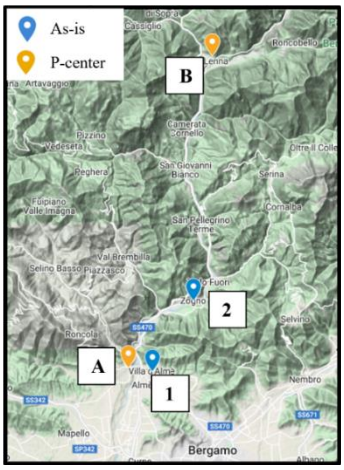

Figure 2. Results of distance minimisation in the "Valle Brembana and Imagna" district.

for the demand (number of frail citizens) of each municipality.The p-median model locates p facilities by minimising the sum of the demand-weighted distance between demand nodes and the nearest of the selected facilities [17]. The objective function of this model is:

$$min \sum_{i=0}^{n} \sum_{j=0}^{n} dist_{ij} \cdot d_i \cdot x_{ij} \tag{7}$$

The advantages of this approach are twofold: i) the real territorial distribution of frail patients is considered and, consequently, the positioning of hubs on the territory follows a patient-centred approach; ii) the selection of small municipalities is avoided by considering the vaccine demand. Considering again the case of the district "Valle Brembana and Imagna", the solution provided by the p-median model would suggest replacing the hub in Valnegra with a new hub located in the municipality of Piazza Brembana, located 2 kilometres from Valnegra. Piazza Brembana is in the valley of the same name; of whose mountain community it is also the main town. Its larger size (around 1200 inhabitants) and the institutional relevance of the municipality in the area make it a strategic point to vaccinate frail citizens. In general, we can state that locating a vaccinal centre in a mountainous area can be beneficial for the fragile population that lives in more remote municipalities of that area, for which it can be complex and/or time-consuming to cover long distances to reach the vaccination centres. Moreover, these difficulties are exacerbated by the fact that such individuals are fragile subjects who often need support from their caregivers. However, even with the p-median model, some hubs could be placed in municipalities lacking adequate infrastructure to accommodate medical facilities. To address these potential criticalities, we updated the p-median model, weighting the demand for an “accessibility index”. It can be developed according to different criteria, and it is a multiplicative factor that reflects how easily a municipality can be reached using a mode of transport at a specific time [18]. The accessibility index that was selected is a multiplication factor α_i ($\alpha_i \in [0,1)\ \forall i \in N$) directly proportional to the number of state roads, provincial roads, and highways crossing the municipalities. Only road transport has been considered as it is the most relevant within the province. The introduction of the accessibility index to weigh the distance favours the selection of easily accessible towns for the hub's location. The objective function of the “modified” p-median algorithm with the accessibility index is now:

$$\min \sum_{i=0}^{n} \sum_{j=0}^{n} (1-\alpha_i) \cdot dist_{ij} \cdot d_i \cdot x_{ij} \qquad (8)$$

Note that $(1-\alpha_i)$ was used as a scaling factor to include a “virtual distance” for each municipality. In other words, if roads well serve a town, it is easier to move from that town to any other municipality of the Bergamo province, and the virtual distance is lower than the actual one. To understand the effect of the accessibility index, we reported the case of the district “East Province”. Positioning the hubs by minimising the demand-weighted distance, one of the district’s vaccination hubs is open in the city of Parzanica (hub 1 in Figure 3). A small town located on the shores of Lake Iseo, simplifying access to vaccination for the frail individuals of that area where there are no vaccination hubs. This configuration is hardly feasible in practice, as the new hub would be open in an area accessible via one provincial road subject to landslides. The introduction of the accessibility index led to replacing the hub in the municipality of Parzanica with a hub in the city of Seriate (hub A Figure 3), which is easier to reach and has a more significant size. However, Seriate is very close to Bergamo, so frail citizens living near the lake would still have to travel many kilometres to reach their vaccinal hub. Introducing the accessibility index sacrifices the optimal geographical positioning of a centre in favour of its easier accessibility. These analyses thus demonstrate how the choice of a single criterion for the location of hubs constitutes an oversimplification of the problem. The application of the p-median model suggests the need to place a vaccination centre on the shores of Lake Iseo to facilitate access for frail patients living in that area. While taking accessibility into account reveals that distance alone does not necessarily influence the ease of accessing the hub, other factors, such as road connections, are important. The policymaker could then look for another town in the area, an alternative to Parzanica, more suitable to host a hub. As the target population changes, the model should also be modified, adapting it to the specific needs of the population under consideration. Ultimately, as is partly to be expected, the optimal solution depends to a large extent on the criterion adopted when comparing the various alternatives.

Figure 3. Results of weighted distance minimisation in the “East Province” district.

B. *Vaccine doses distribution*

The vehicle routing problem aims to identify the optimal routes to be travelled by a fleet of vehicles for the delivery and distribution of goods [19]. For the case study, we implemented the capacitated periodic VRP with time constraints. In fact, vehicles have a limited storage capacity. In classical VRPs, typically, the planning period is a single day. In the case of the Periodic Vehicle Routing Problem (PVRP), the VRP is generalised by extending the planning period to T day [20]. In our case study, the delivery covers a horizon of four working days. The sum of the travel and discharge times at each vaccinal hub should be lower than a working day (assumed equal to 8 hours). We assumed a collaborative transportation approach; therefore, the vehicle is shared between the three health authorities and it delivers to all hubs regardless of their health authority of origin. Let $T = 1, \dots, m$ be the planning horizon, $V = 1, \dots, n$ be the set of vaccinal hubs including the central depot identified with the label 1, $N = V \setminus \{1\}$ be the set of vaccinal hubs excluding the central depot, C be the capacity of the vehicle, d_i be the demand of each vaccinal hub, $dist_{ij}$ be the distance between municipalities i and j $(i, j \in V)$ and u_i^t be an integer variable that define the order of nodes $(i \in V, t \in T)$. Let tt_{ij} be the time required to move from centre i to centre $j\,(i, j\ \in V)$ assuming an average speed of 70km/h and let dt_j be the time required to unload the ordered vaccine doses at the vaccination centre $j \in V$. The decision variables are:

$$x_{ij}^t = \begin{cases} 1 \ iff\ vehicle\ visit\ hub\ j\ after\ hub\ i\ on\ day\ t \\ 0 \quad otherwise \end{cases}$$

$$z_i^t = \begin{cases} 1 \ iff\ hub\ i\ is\ visited\ on\ day\ t \in T \\ 0 \quad otherwise \end{cases}$$

While the objective function is:

$$min \sum_{i=0}^{n} \sum_{j=0}^{n} c_{ij} \sum_{t=1}^{m} x_{ij}^t \qquad (9)$$

Function (9) is the minimisation of the travel cost throughout interest T, subject to:

$$\sum_{i \in V} \sum_{j \in V} d_i x_{ij}^t < C \quad \forall t \in T \qquad (10)$$

$$\sum_{t \in T} z_i^t = 1 \ \forall i \in N \qquad (11)$$

$$\sum_{t \in T} z_1^t \leq 4 \ and \ \sum_{t \in T} z_1^t \geq 1 \qquad (12)$$

$$\sum_{t \in T} \sum_{i \in V,\ i \neq j} x_{ij}^t = 1, \forall j \in N \ and \quad \sum_{t \in T} \sum_{j \in V,\ i \neq j} x_{ij}^t = 1, \forall i \in N \qquad (13)$$

$$x_{ii}^t = 0, \qquad \forall i \in V, \forall t \in T \qquad (14)$$

$$\sum_{j \in N} x_{ij}^t = z_i^t, \forall i \in V, \forall t \in T \qquad (15)$$

$$u_i^t - u_j^t + (n-1) \cdot x_{ij}^t \leq n-2, \ \forall i,j \in V, \forall t \in T \qquad (16)$$

$$\sum_{j \in V} \sum_{i \in V} x_{ij}^t \left(tt_{ij} + dt_j \right) \leq 480 \ \forall t \in T \qquad (17)$$

$$x_{ij}^t \in \{0,1\}, \forall i,j \in V, \forall t \in T \ and\ z_i^t \in \{0,1\}, \forall i \in V, \forall t \in T \qquad (18)$$

Constraint (10) imposes that the total quantity delivered by the vehicle on day t must not exceed the vehicle's capacity C. Constraint set (11) imposes that exactly one delivery for each hub is planned over the time horizon. Constraints (12) verify that the vehicle must start its daily route at the central depot. Additionally, a vehicle visits each hub once over the time horizon (13), and arcs (i,i) are not viable (14). Constraint set (15) verifies that each client is visited exactly on the planned day. Constraint (16) imposes that no sub-tours are allowed, and (17) imposes that the sum of travel time and unloading time at the centres does not exceed a working day. Constraint set (18) bounds the variables domain. Unlike the current organisation where deliveries are made in four days, the application of the periodic VRP with time constraints returns a solution which includes two delivery days: Monday and Tuesday. To test the robustness of these results, we varied the average travel speed reducing it to 50km/h and the unloading time at each hub between 15 and 30 minutes. In all cases, delivery to the hubs was completed within two days. Indeed, given the province of Bergamo's modest size, it is plausible to believe that all hubs can be covered in just two days. This result shows that, on average, the actual distribution routes are under-utilised and not operating at full capacity. Consequently, collaboration plays an important role in transportation system optimisation; resource sharing can be utilised in collaborative logistics networks to increase resource utilisation. Combining the distribution routes to the hubs, independently from the health authority to which they belong, makes it possible to reduce the delivery horizon. Free days can be used for deliveries of other products or to plan additional deliveries. However, this approach may be complex due to the organisational fragmentation of the three health authorities.

V. DISCUSSION

The results obtained through the implementation of the described models differ in many cases from the settings of the as-is vaccination hubs' organisation. In some cases, such differences are not negligible since they simplify access to vaccination, especially for frail subjects living in more remote areas of the Bergamo province. This result implies that, on average, by implementing the solutions provided by the *p*-center or the *p*-median model, frail citizens would travel a shorter distance to reach vaccination hubs. However, the proposed solutions are not always feasible. In some cases, minimising the distance between patients and vaccination hubs leads to the location of hubs in municipalities that are difficult to access and lack the necessary infrastructure. The introduction of the accessibility index has helped to curb this problem. The presented case study demonstrated how the selection of one facility location algorithm over another produced distinct solutions, each with its own set of advantages and disadvantages. As a result, it enabled the collection of suggestions on how to enhance the current system to promote immunisation access for frail citizens, coupled with considerations regarding the feasibility of the vaccination network. Regarding the distribution of vaccines, the solution obtained through optimisation models differs from the one currently implemented in the province. This solution increases the system's effectiveness, allowing all doses to be delivered quickly. Furthermore, on days when deliveries are not scheduled, additional delivery routes can be planned. However, the current organisation of deliveries based on four working days is caused by the lack of collaboration between the three public territorial health companies, which organise deliveries independently. This choice results in the underutilisation of vehicle capacity. As a result, the implementation of collaborative vaccine distribution would be beneficial but may be challenging to implement. Again, the case study offers suggestions for improving vaccine distribution organisation, but theoretical results must be combined with qualitative assessments of their feasibility. It is fundamental to highlight how solutions provided by the models should not be accepted a priori. Both regarding hub location and vaccine distribution, the optimal solution depends to a large extent on the criterion adopted when comparing the various alternatives. This result leaves room for considerations that should be placed alongside the quantitative analysis, which, by its very nature, can hardly take into account all the factors, often qualitative, that drive the final decision and may imply organisational trade-offs.

VI. CONCLUSIONS

These analyses demonstrated the importance of using location algorithms as a strategic and effective support for decision-makers. Indeed, the simple models used provided recommendations on how to improve the organisation of the vaccination network from the frail individuals' point of view regarding facility location and vaccine doses distribution. However, the results provided by models are not always optimal, particularly regarding models using a single location criterion; they must be supplemented by human considerations regarding their feasibility. The main limitations of this paper are the single case study approach. Future research in this area would benefit from a multiple-case approach, not only in the healthcare sector, considering other types of rural areas or target citizens (i.e., children vaccination). Other suggestions for improvement could be gathered from applying additional optimisation algorithms. An example could be to consider the capacitated *p*-median problem: associating a capacity with each hub to deal with the maximum allowed size of a hub. In this way, even small villages could receive a hub, but these (small) hubs would be allowed to serve only a small amount of demand, i.e., the number of nearby villages. Alternatively, other accessibility index formulations could be applied.

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