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Research on the Location Selection and Path Optimization of Pharmaceutical Distribution Centers Considering Supply Chain Resilience

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Abstract: This study explores the location-routing optimization for pharmaceutical cold chain distribution, addressing the challenges of supply stability and efficiency. A dual-objective model minimizing cost and time is proposed, incorporating supply chain resilience. An improved NSGA-II algorithm based on multiverse theory enhances solution quality and convergence. Using real data from South China, the study analyzes distribution center resilience and reveals trade-offs via Hyper Volume analysis. The findings support practical decision-making and enhance supply chain reliability.

Keywords: Dual objective optimization; Supply chain resilience; Pharmaceutical transportation; NSGA-II Algorithm.

1. Introduction

APharmaceutical logistics falls under the category of cold chain logistics. It involves the entire circulation process of refrigerated pharmaceutical items such as medicines, vaccines, and IVD (in vitro diagnostic products), covering their entire life cycle from raw material storage, production, semi-finished processing, packaging, storage, transportation, distribution to sales. The core requirement of pharmaceutical logistics is to ensure that the transported items are kept within a specific low-temperature range. Therefore, pharmaceutical logistics is a subcategory of cold chain logistics with relatively stringent low-temperature refrigeration requirements.

In 2022, despite facing multiple challenges, China's pharmaceutical logistics industry demonstrated a trend of recovery and growth. The pharmaceutical distribution market size increased by 6.3% year-on-year, reaching approximately 2.8 trillion yuan, indicating a steady market recovery. The total pharmaceutical logistics cost also grew by 5.7%, mainly due to the stable growth of the pharmaceutical manufacturing and distribution industries and the rapid development of online pharmaceutical sales. The pharmaceutical logistics warehousing area expanded by 3.0%, showing a recovery and improvement in the modernization capability of pharmaceutical logistics warehousing construction. The number of pharmaceutical logistics vehicles increased by 3.5%. Although the growth rate was relatively small, it became an inevitable trend with the expansion of the market scale. Moreover, vehicles are evolving towards being lightweight, having larger space, and achieving more precise temperature control.

Influenza vaccine transportation is an important branch of pharmaceutical logistics research. Influenza is an acute respiratory infectious disease caused by the influenza virus, which is highly contagious and variable. It can cause seasonal outbreaks every year, posing a serious threat to human health. The World Health Organization estimates that influenza causes 3 to 5 million severe cases and 290,000 to 650,000 respiratory disease-related deaths globally each year. According to the "Estimation of Seasonal Influenza Disease Burden in China from 2006 to 2019" published in the Chinese Medical Journal in 2021, the average annual number of influenza cases in China is 3 million for outpatient and emergency visits and 2.34 million for hospitalizations. Vaccination against influenza is the most cost-effective measure to prevent the disease, as it can reduce the chance of infection or alleviate the symptoms of influenza for those who are vaccinated. With the development of the medical system and the gradual improvement of the pharmaceutical supply chain, the coverage and scale of the medical drug supply network are expanding. This also makes the pharmaceutical supply network more susceptible to external risk factors such as natural disasters and human destruction. To cope with the negative impact of uncertain external risk factors on the large-scale pharmaceutical supply network, ensuring the reliability and cost-effectiveness of the pharmaceutical supply network has become a key issue.

This paper, from the perspectives of reliability and cost-effectiveness, uses a location-routing model and an improved NSGA-II algorithm to determine the supply chain resilience of each candidate distribution center, as well as the corresponding total transportation cost and total delivery time Pareto solutions. Establishing location-routing optimization strategies for each candidate point around the supply reliability and cost-effectiveness of influenza vaccines can improve the efficiency of supply network analysis and improvement, and has greater practical application value..

2. Literature review

2.1. Overview of the Pharmaceutical Supply Chain

The pharmaceutical supply chain is a complex network system, which encompasses multiple entities ranging from raw material suppliers, research and development institutions, drug manufacturers, logistics service providers, wholesalers, retailers to medical institutions and end patients. These entities are interconnected through logistics, information flow and capital flow, jointly completing the entire process of drugs from production to delivery to consumers. With the development of The Times, this concept has been constantly enriched and improved.

Initially, the pharmaceutical supply chain mainly focused on the production and distribution links of drugs, regarding it as an internal production activity of the enterprise. With the integration of the global economy, the scope of the pharmaceutical supply chain has gradually expanded to cross-enterprise networks, with greater emphasis on cooperation and information sharing among enterprises. After entering the 21st century, the pharmaceutical supply chain has further developed into a more complex network, with greater emphasis on the coordination and cooperation among suppliers, manufacturers, distributors, retailers and end users.

The demand for the pharmaceutical market is jointly influenced by multiple factors such as seasonal changes, disease epidemic trends, adjustments in medical insurance policies, and public health emergencies, thus presenting obvious fluctuations and uncertainties. In the typical case of influenza vaccines, during the high-incidence season of influenza, due to the rising infection rate and the enhanced public awareness of prevention, its demand usually increases sharply, while it remains relatively stable during the non-high-incidence period. This phenomenon indicates the important role of seasonal factors in the demand for medicine. Meanwhile, adjustments to medical insurance policies (such as changes in the scope, amount and payment ratio of medical insurance reimbursement, etc.) will also affect the actual demand for medical products, causing the demand structure to adjust along with changes in the policy environment. In addition, public health emergencies (such as the COVID-19 pandemic) can also have a significant impact on the pharmaceutical supply chain, leading to a sharp increase in demand for certain drugs while a sharp decrease in demand for others [1].

Many scholars have also conducted innovative research on the pharmaceutical supply chain. Xu et al. [2] studied the drug cold chain location-routing problem (MFLRPPCCL) for hybrid energy vehicles, constructed a multi-objective optimization model considering uncertain factors such as carbon emissions, fuzzy demand, travel time and energy consumption, and solved it using the NSGA-II algorithm. By introducing temporary distribution centers and various reliability constraints, the variation laws of cold chain logistics routes and costs under uncertain conditions were systematically analyzed. The research of Rong et al. [3] proposed a service quality evaluation framework based on the q-rung orthopair fuzzy set, integrating the improved DEMATEL method and classification method, and achieving uncertainty processing and weight distribution under multiple experts and multiple criteria. It innovatively constructed a game theory combined weight model integrating subjective and objective weights, and introduced a new distance measurement method to enhance the scientificity and stability of the evaluation of the service quality of drug cold chain logistics. The research of Seung and Byung[4] aimed at the order acceptance problem in the cold chain distribution of drugs and constructed a mixed integer linear programming model considering the storage temperature and shelf life requirements to maximize the total profit. A hybrid genetic algorithm of embedding insertion heuristic and modification operation is proposed, and the order acceptance strategies in different environments are explored through sensitivity analysis, which has strong practical value and optimization ability. Finally, Aura et al. [5] studied the uncertain demand problem in the Brazilian pharmaceutical logistics network, constructed an integrated optimization model of location and transportation including multi-time-scale decisions, and introduced robust optimization methods to deal with uncertainties. The innovation lies in combining the Fix-and-Optimize heuristic algorithm with actual enterprise data, significantly reducing logistics and tax costs, and improving the adaptability and practicability of site-transportation decisions.

2.2. Characteristics of location selection and path optimization in the pharmaceutical supply chain

The location selection - path optimization model of the pharmaceutical supply chain has high complexity and multi-dimensionality. When constructing such models, many variables and parameters need to be considered, which involve all links and levels of the pharmaceutical supply chain. For example, in the case of uncertain demand, the model should not only consider the demands of producers, distributors and customers, but also take into account multiple factors such as transportation costs, production costs and storage costs simultaneously.

The location selection and path optimization model of the pharmaceutical supply chain usually involves multiple optimization objectives, and there are often conflicts among these objectives, which need to be balanced. Common optimization goals include minimizing costs, maximizing service levels, minimizing total transportation time, and enhancing supply chain resilience, etc. Although each goal has its own focus, they often restrict each other in actual operation. For example, pursuing the lowest operating costs may affect the delivery speed or service quality, while improving the service level and shortening the total transportation time may bring additional costs; Meanwhile, the improvement of supply chain resilience not only involves the trade-off between cost and time, but also takes into account the emergency response capability and stability of the entire system in the face of sudden risks. Decision-makers must make comprehensive considerations and trade-offs among these optimization objectives in the actual decision-making process. They should not only ensure the efficiency and reliability of logistics operations but also take into account the overall goals of the enterprise, so as to find the solution that best suits the interests of the enterprise. In past studies, when constructing the operation model of the pharmaceutical supply chain, the NSGA-II algorithm was usually used to comprehensively consider the two core goals of operation cost and service level, construct a multi-objective optimization model, and solve it using this algorithm. This method can generate multiple solutions simultaneously, providing decision-makers with a set of non-dominated Pareto optimal solutions to help them conduct comprehensive evaluations and choices from different perspectives such as cost, time, service and resilience. Meanwhile, this type of multi-objective optimization method not only highlights the balance effect among various objectives, but also significantly improves the adaptability and stability of the model when dealing with practical problems. This method reflects the advantages of modern optimization algorithms in the location selection and path optimization problems of the pharmaceutical supply chain, providing decision support for dealing with the complex operating environment and changing market demands, and also laying a theoretical foundation for the subsequent in-depth study of the trade-off mechanism among different optimization objectives. Through this comprehensive multi-objective optimization strategy, managers of the pharmaceutical supply chain can better grasp the balance among various key indicators, thereby ensuring efficient and stable logistics distribution in actual operation while creating greater economic benefits and competitive advantages for the enterprise.

2.3. Characteristics of location selection and path optimization in the pharmaceutical supply chain

To enhance the resilience of the pharmaceutical supply chain, modern enterprises have adopted a variety of measures. Strengthening the application of digital technologies is one aspect: introducing new technologies such as big data, artificial intelligence and blockchain to achieve visual and intelligent management of the pharmaceutical supply chain and enhance the transparency and collaboration efficiency of the supply chain. Secondly, optimize the layout of the supply chain. Rationally plan the location selection of production, distribution and warehousing facilities for pharmaceutical enterprises to avoid risks brought about by excessive concentration and establish a diversified supply chain network. In addition, efforts should be made to enhance cooperation, promote information sharing, resource integration and business synergy among enterprises in the upstream and downstream of the pharmaceutical supply chain, and form close cooperative relationships and collaborative effects. Furthermore, improve the emergency management system, establish a complete emergency plan and mechanism for the pharmaceutical supply chain, and be able to promptly activate the response and take effective measures for handling and recovery when emergencies occur. Finally, promoting the green and low-carbon development of the supply chain is also an effective approach. Implementing the concept of green development in all links of the pharmaceutical supply chain, optimizing the energy structure, reducing environmental pollution, and achieving sustainable development. Through these measures, pharmaceutical enterprises can enhance the risk-resistance capacity and stability of their supply chains to adapt to the ever-changing market environment and the growing demand for pharmaceuticals. Specifically, enterprises should increase their investment in digital technologies, establish a unified data platform, and achieve immediate information sharing and collaborative management among all links of the supply chain. Meanwhile, by optimizing the supply chain layout and diversifying risks, the stability and reliability of the supply chain in the event of emergencies can be ensured. Strengthen close collaboration with suppliers and logistics partners, establish long-term and stable strategic partnerships, and jointly respond to market changes and risk challenges. In addition, the government should also enhance its support for the pharmaceutical supply chain, provide policy guidance and financial support, and promote the innovation and development of the supply chain. Through the joint efforts of all parties, a more risk-resistant and sustainable pharmaceutical supply chain system should be constructed to provide reliable guarantees for public health and social stability [6].

3. Methodology

3.1. Problem description

The problem studied in this paper can be described as follows: In the cold chain logistics distribution of medicine, there are several demand points with fixed geographical locations, and one of them needs to be selected as the distribution center for construction. In addition, they need the distribution center to complete the distribution tasks of medical products within the prescribed time window. The distribution demand is known, and the distribution center has a sufficient number of medical transportation vehicles of the same model and equipped with refrigeration devices. Medical transport vehicles need to depart from the distribution center, complete all distribution tasks and then return to the distribution center for maintenance.

During the delivery process, the following requirements must be met: the vehicle's load capacity must not exceed the maximum limit, the customer's demands must be met at one time, and the total cost must be minimized. The total cost includes vehicle fixed cost, transportation cost, time window penalty cost, refrigerant consumption cost and facility construction cost. The goal is to reduce the total cost and the total delivery time by optimizing the location of the distribution center and the transportation routes of vehicles. The optimization effect diagram of the site-path model for pharmaceutical logistics is shown in Figure 1.

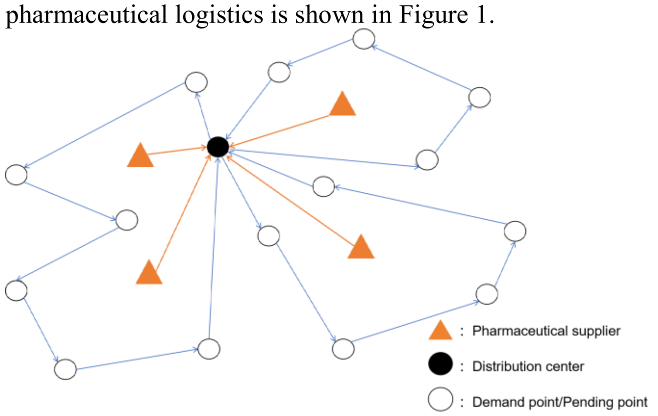

Figure 1. Location - route model optimization of pharmaceutical logistics

3.2. Assumptions

We make the following assumptions to construct a dual-objective optimization model for the location selection and path optimization of the medical distribution center:

1)The distribution center is of a single source and serves multiple customer points.

2) Medical transport vehicles do not need to be fully loaded when setting off.

3) All delivery tasks use the same model of medical transport vehicles, and the number of such vehicles is sufficient.

4) The vehicle's refrigeration equipment operates stably, maintaining a constant temperature both inside and outside the compartment, and is not affected by road traffic conditions.

5) The customer's geographical location, demand volume and time window requirements are known and fixed.

3.3. Model Establishment

3.3.1. 3.3.1 Symbol Explanation

(1) Set

For the set of customer points, V={1,2,3,... n};

For the collection of refrigerated delivery vehicles, K={1,2 ,3,... m}.

(2) Parameters

c_1: The fixed operating cost of each medical transport vehicle;

c_2:The transportation cost per unit distance traveled by a medical transport vehicle;

c_3:Waiting cost per unit time

c_4:Penalty cost per unit time

c_5:Refrigerant cost per unit weight

Q:The maximum load capacity of medical transport vehicles;

d_{ij} :Distance between customer points

t_{ij} :The time required from customer point to customer point;

q_i :The demand for medicine at the customer's point;

t_i : The time required for the medical transport vehicle to unload at the customer's point;

f : Fuel consumption function

α_1 : The proportion of medical drug losses during transportation;

α_2 : The proportion of medical drug losses during the unloading process;

$\left[ET_i, LT_i\right]$:The time window of the customer's order.

U_i:The freight carrying capacity when selecting demand point i as the distribution center.

(3) Decision variables

t_i^k :The time when the medical transport vehicle k arrives at the customer's location;

$t_i^{k'}$:The time when the medical transport vehicle k leaves the customer point;

Q_{ij}^k :The loading capacity of the medical transport vehicle k on the arc;

X_{ij}^k :Variable: 0-1. If =1, it indicates that the medical transport vehicle k passes through an arc; otherwise, it is 0.

Y_i^k :Variable: 0-1. If =1, it indicates that the medical transport vehicle k serves customer point i; otherwise, it is 0.

DC_i :For the 0-1 variable, if =1, it indicates that the demand point i is selected as the distribution center; otherwise, it is 0.

3.4. Objective Function Analysis

3.4.1. Fixed cost

During the distribution process, the fixed cost can be expressed as:

$$Z_1 = c_1 \sum_{k\in K} \sum_{i\in V} \sum_{\substack{j\in V: \\ j\neq i}} X_{ij}^k \cdot DC_i \tag{1}$$

3.4.2. Transportation cost

Transportation costs are mainly determined by the amount of fuel consumed during vehicle transportation. Transportation costs can be expressed as:

$$Z_2 = c_2 \sum_{k\in K} \sum_{i\in V} \sum_{\substack{j\in V: \\ j\neq i}} d_{ij} X_{ij}^k \tag{2}$$

3.4.3. Time window cost

When the vehicle fails to complete the service within the time range specified by the customer, the penalty cost will be incurred as follows:

$$Z_3 = c_3 \sum_{k\in K} \sum_{i\in V} \max\left\{ET_i - t_i^k, 0\right\} Y_i^k + c_4 \sum_{k\in K} \sum_{i\in V} \max\left\{t_i^k - LT_i, 0\right\} Y_i^k \tag{3}$$

3.4.4. Refrigeration cost

The refrigeration cost is expressed during transportation as:

$$Z_{41} = c_5 g_1 \sum_{k\in K} \sum_{i\in V} \sum_{\substack{j\in V: \\ j\neq i}} t_{ij} X_{ij}^k \tag{4}$$

3.4.5. Construction fixed cost

For demand point i, its construction fixed cost is:

$$Z_5 = \sum_{i\in V} FC_i \cdot DC_i \tag{5}$$

3.5. Resilience index

Resilience indicators, as a group of important indicators independent of the dual-objective optimization model, after measuring each demand city using the resilience quantification model, can be combined with the dual-objective solution set through the Hyper Volume three-dimensional view, in order to achieve the effect of comprehensive trade-off. Therefore, when constructing this paper, based on the theoretical framework of scholars who have studied supply chain resilience in the past, data at the production (vaccine production capacity ratio), economic (fiscal subsidies), and social (urban GDP) levels of the city were collected to comprehensively depict the impact of cold chain facilities, geographical location, and production capacity on the resilience of the pharmaceutical supply chain, providing useful references for management decisions.

Firstly, when analyzing the resilience of the pharmaceutical supply chain, considering the inconsistent dimensions of urban economic data and the distances between cities, it is necessary to appropriately handle the distance from the demand point to the supplier, so that in the subsequent calculation, the mutual influence of the economic and geographical distribution between different demand points and suppliers can be measured more intuitively and uniformly. For this purpose, the normalization processing method is usually adopted to map the distance values to the dimensionless interval of [0,1]. Specifically, first find the minimum and maximum values in the set of distances from all the available demand points to the suppliers, and then linearly normalize the distances using the following formula:

$$L_{ir\ norm} = \frac{L_{ir} - L_{min}}{L_{max} - L_{min}} \tag{6}$$

On the basis of obtaining the normalized distance, the supply chain resilience parameters can be further constructed to measure the comprehensive adaptability and anti-interference ability of the supply chain when facing various potential risks and uncertainties. In this model, multi-dimensional data such as geographical location distribution, urban economic indicators, fiscal input for cold chain, and supplier production capacity are combined. The overall resilience value E_{ir} corresponding to each demand point i is obtained through weighting and summary methods, which is specifically expressed as:

$$E_{ir} = \frac{\sqrt{\frac{Q_i}{G_i} \cdot \frac{Q_r}{G_r}}}{L_{ir\ norm}} \cdot e^{-[1-(1+\mu_i)^{\sum y_r}(1-\sum_{r\in R} S_{ir} \cdot y_r)]} \tag{7}$$

In conclusion, the mathematical model of the cold chain VRPSPDTW constructed in this chapter is as follows:

Minimize the total cost:

$$min\, Z = Z_1 + Z_2 + Z_3 + Z_4 + Z_5 \tag{8}$$

Minimize the delivery completion time

$$min\, T = \sum t_i + (t_i^{k'} - t_i^k) + t_{ij} \tag{9}$$

Constraint

$$\sum_{k \in K} Y_i^k = 1, \forall i \in V \tag{10}$$

$$\sum_{i \in U} X_{ij}^k = Y_j^k, \forall j \in V, \forall k \in K \tag{11}$$

$$\sum_{j \in U} X_{ij}^k = Y_i^k, \forall i \in V, \forall k \in K \tag{12}$$

$$\sum_{i \in V} \sum_{\substack{j \in V: \\ j \neq i}} X_{ij}^k \cdot DC_i = \sum_{i \in V} \sum_{\substack{j \in V: \\ j \neq i}} X_{ji}^k \cdot DC_i = 1, \forall k \in K \tag{13}$$

$$\sum_{j \in V} Q_{0j}^k = \sum_{i \in U} q_i Y_i^k, \forall i \in V, \forall k \in K \tag{14}$$

$$\sum_{k \in K} \sum_{i \in V} Q_{ij}^k = \sum_{k \in K} \sum_{i \in V} Q_{ji}^k - q_i, \forall j \in V \tag{15}$$

$$0 \leq Q_{ij}^k \leq Q, \forall i \in U, \forall j \in U, \forall k \in K \tag{16}$$

$$t_i^k + max\{ET_i - t_i^k, 0\} + t_i = t_i^{k'}, \forall i \in V, \forall k \in K \tag{17}$$

$$t_i^{k'} + t_{ij} = t_j^k, \forall i \in U, \forall j \in U, i \neq j, \forall k \in K \tag{18}$$

$$\sum_{k \in K} \sum_{i \in V} \sum_{\substack{j \in V: \\ j \neq i}} Q_{ij}^k \cdot DC_i \leq U_i \tag{19}$$

$$\sum DC_i = 1 \tag{20}$$

$$X_{ij}^k \in \{0,1\}, \forall i \in U, \forall k \in K \tag{21}$$

$$Y_i^k \in \{0,1\}, \forall i \in U, \forall k \in K \tag{22}$$

In the model, Equation (3.10) stipulates that each customer can only receive the delivery service once, ensuring the unique allocation of the delivery task, avoiding repetition or omission, and thus ensuring the feasibility of the model in actual implementation. Equations (3.11) and (3.12) construct the logical constraints among the decision variables, reflecting the changes and sequence relationships of the loading capacity of the vehicle among different customer points, enabling the load state of the vehicle after unloading to truly reflect the actual situation. Equation (3.13) clearly requires that each distribution vehicle must return to the distribution center after completing all customer tasks. This constraint is consistent with the actual cold chain distribution requirements. Immediately afterwards, Equation (3.14) ensures that the amount of goods loaded by the vehicle at departure precisely matches the total demand of customers along the way to achieve a balance between supply and demand. Equation (3.15) describes the dynamic changes of the vehicle's load capacity before and after passing through customer service. Equation (3.16) imposes an upper limit on the vehicle loading capacity. This constraint is set based on the technical parameters and transportation requirements of cold chain vehicles to ensure that the optimization results comply with the actual transportation conditions. For the service schedule arrangement, Equations (3.17) and (3.18) are used to ensure a reasonable connection of the arrival and departure times of vehicles at each customer point. While meeting the requirements of the time window, they maintain the continuity of the service and take into account the time required for unloading. Equation (3.19) stipulates that the total load capacity of all vehicles departing from the distribution center shall not exceed the carrying capacity of the distribution center. Equation (3.20) limits that the system can only build a single distribution center to avoid the repetitive construction of multiple centers. Finally, Equations (3.21) and (3.22) respectively define the value ranges of the two decision variables.

Overall, these constraints together form the core framework of the VRPSPDTW mathematical model for cold chain. By comprehensively considering key factors such as vehicle capacity, time window constraints, distribution routes, and resilience, an accurate description of the actual pharmaceutical cold chain distribution process has been achieved, and a solid theoretical foundation has been provided for subsequent optimization solutions.

4. Improved Design of NSGA-II Algorithm

4.1. Improved INSGA-II algorithm

In the traditional NSGA-II algorithm, the population initialization stage often adopts a single random generation method. This method limits the maintenance of population diversity to a certain extent and is prone to cause the initial solution to be unevenly distributed in the search space, thereby making the algorithm more likely to fall into local optimum in the subsequent evolution process.

To solve the problems existing in the population initialization stage of the traditional NSGA-II algorithm, this paper introduces the multiverse algorithm MVO (Multi-Verse Optimization) to improve the NSGA-II algorithm, which is marked as the "INSGA-II algorithm" below.

The Multiverse Algorithm (MVO) simulates the evolution mechanisms of white holes, black holes, and wormholes in cosmology, treating each solution as a "universe" and exploring and developing in the space of solutions by simulating the mechanisms of "white holes", "black holes", and "wormholes". A white hole represents the current optimal solution injecting information into other solutions, a black hole represents the replacement of a poorer solution, and the wormhole mechanism gradually focuses the search on the optimal region by setting the probability of existence (WEP) and the transmission distance (TDR). The simulation results show that this method is superior to mainstream algorithms such as VSA, CSA, and PSO in terms of convergence speed and solution stability, demonstrating strong adaptability and optimization ability in complex problems.

4.2. The improved INSGA-II algorithm process

In multi-objective optimization problems, the improved INSGA-II algorithm combines the advantages of the traditional NSGA-II algorithm with the idea of the multiverse, achieving more efficient global search and local fine optimization (the specific flowchart of the improved INSGA-II algorithm is shown in Figure 4.8 below).

The algorithm first generates the initial population through the multiverse initialization method in multiple independent subspaces and calculates the fitness respectively, thereby ensuring the diversity of the solutions and avoiding local convergence. Next, the non-dominated sorting technique is used to hierarchically sort the entire population. The individual priorities are determined based on the performance of each target, and at the same time, excellent solutions with distinct characteristics are retained in each "universe".

In the selection stage, the algorithm adopts a cross-universe selection strategy to select the parent generation with higher adaptability from different subspaces, enabling the integration of multi-domain information. Subsequently, in the improved crossover and mutation operations, the individual information of the parent generation is deeply integrated, which not only inherits the local excellent characteristics but also enhances the global exploration ability of the group. The environmental selection stage is based on the cross-universe update strategy, merging the parent generation and the offspring generation. By dynamically eliminating low-quality individuals, the population structure is continuously optimized.

Finally, the convergence of the algorithm is detected through multi-dimensional termination conditions. If the preset criteria are met, the optimal solution set is output; otherwise, the iteration continues. This improved scheme not only enhances the solution quality and convergence speed, but also ensures the population diversity. It has high robustness and practical value, providing a brand-new technical path for solving complex multi-objective problems.

5. Analysis of Numerical Examples

5.1. Test environment and test data

In order to verify the effectiveness of the improved strategy in enhancing the performance of the NSGA-II algorithm, this study adopts the empirical research data of Hou Feifei [3] on the cold chain distribution of Company S. The correlation coefficients of various costs in the model are consistent with the actual situation of Company S. On this basis, in order to meet the transportation requirements of vaccines, the parameters of the transportation vehicles were adjusted, and medium-sized Iveco cold chain transport vehicles (with dimensions of 5995mm×2000mm×2800mm, load capacity of 1.8 tons, and maximum volume of 8.5m³) were selected. Meanwhile, combined with the subsidy amounts for the construction of cold chain distribution centers released on the official websites of municipal governments in China, the real GPS coordinates of the cities, and the financial data of four major vaccine manufacturing enterprises in South China, a simulation scenario of vaccine cold chain transportation under real scenarios was constructed to verify the scientificity of the site-path dual-objective optimization model considering supply chain resilience proposed in this paper.

5.2. Analysis of Actual Cases

In order to be closer to the actual operation situation of cold chain transportation, the transportation parameters adopted in this paper partially refer to the empirical analysis data of the cold chain distribution center of Company S conducted by Master Hou Feifei in her research. This data covers the cold chain transportation business of Company S, which serves 306 customers in 15 distribution areas. As a professional enterprise specializing in third-party logistics services, Company S has highly professional and reliable data related to cold chain transportation. The research of Master Hou Feifei mainly focuses on the planning problem of optimizing the cold chain distribution route of Company S, providing important empirical support for this paper. Its parameter Settings are shown in Table 1. as follows.

Table 1. Model parameter Settings

parameter	Parameter value	parameter	Parameter value	parameter	Parameter value
c_1	160 Yuan/per unit	c_7	1 Yuan/kg	α_2	0.003
c_2	6 Yuan/km	ρ_0	0.165L/km	β	0.08
c_3	0.33 Yuan/min	ρ^*	0.377L/km	R	2.49k$Cal/(h*m^2*{}^{\circ}C)$
c_4	0.5 Yuan/min	σ_1	2.63kg/L	γ	1
c_5	0.02 Yuan/kg	σ_2	0.0066kg/min	T_w	21
c_6	1.5 Yuan/kCal	α_1	0.002	T_n	4

We quantified the resilience value of each demand point city when it was used as a distribution center, and sought the Pareto optimal solution of each demand point city when it was used as a distribution center, obtaining a total of 83 site-distribution optimization schemes in 15 groups. Among them, the total transportation time of the No. 18 site selection - route optimization scheme with Meizhou City as the distribution center was the lowest, which was 598.83. The average daily total transportation cost of the No. 23 site selection - route optimization scheme with Heyuan City as the distribution center was the lowest, which was 121,777.57 yuan. The vaccine cold chain transportation resilience value with Zigong City as the distribution center was the highest, which was 0.1000. This set of optimization plans provides a scientific basis for the regional cold chain logistics distribution of vaccines and has important practical significance.

The three-dimensional view of Hyper Volume made based on the data in the above table is shown in **Figure 2.** as follows:

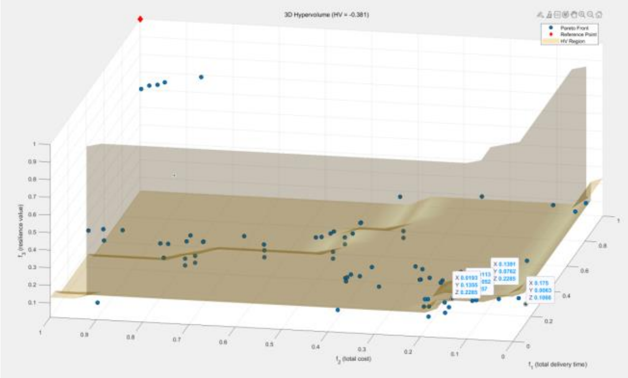

Figure 2. Optimization scheme Pareto solution set hyper volume graph

As shown in **Figure 2.** , first of all, from the perspective of the trade-off between the total transportation cost and the total distribution time, we selected four groups of high-quality Pareto solutions for in-depth analysis. By observing the hyper volume graph, it can be found that these solutions show obvious nonlinear characteristics in the distribution of cost and time, indicating that there is a significant multi-objective trade-off relationship in the optimization process. Further combined with the resilience values/longitudinal section analysis in **Figure 4.**, the differences in resilience values among different Pareto frontier solutions can be observed, which provides a crucial analytical perspective for the site-path decision in supply chain management.

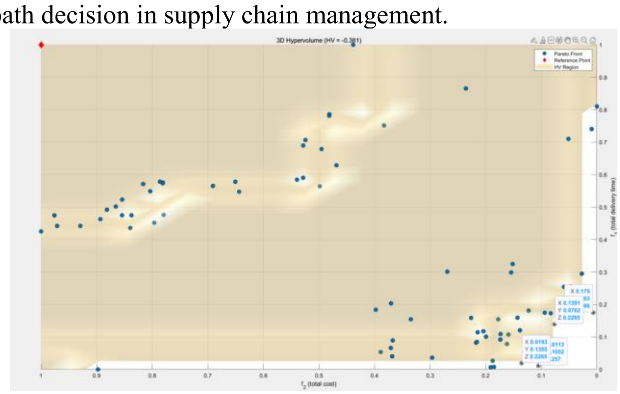

Figure 3. Hyper volume diagram of Pareto solution set (toughness value/longitudinal section)

Figure 3. shows the distribution of Pareto solutions from the perspective of the cost and time sections. It can be seen that as the total transportation cost decreases, the total delivery time shows a certain degree of fluctuation, which indicates that the balance between cost and time needs to be comprehensively considered in the optimization process. Especially in areas with low transportation costs, the fluctuation range of the total delivery time is relatively large, indicating that there may be multiple optimized path options within this area. Decision-makers need to balance the priorities of time and cost based on actual needs.

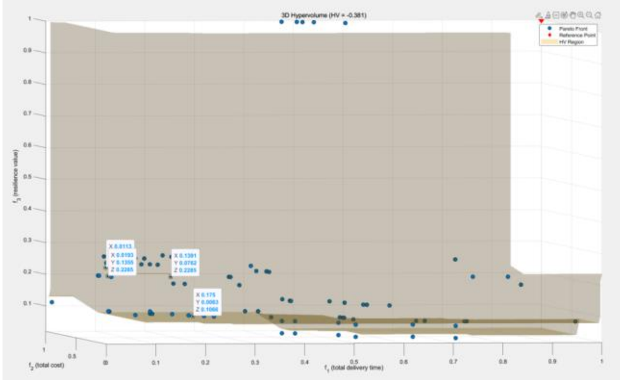

Figure 4. Hyper volume diagram of Pareto solution set (toughness value/longitudinal section)

Figure 4. further analyzes the characteristics of the Pareto solution from the perspective of the toughness value/longitudinal section. The results show that the differences in resilience values among different solutions are significant. Especially in the area with high resilience values, the distribution of solutions is relatively sparse, indicating that optimization is more difficult in this area. In the area with low resilience values, the distribution of solutions is relatively dense, indicating that there are more optimization possibilities in this area. In addition, the three demand points of Guiyang City, Qiannan Prefecture and Suining City, due to their remote geographical locations, insufficient financial subsidies for cold chain, and limited influence of the city's size at supply chain nodes, have resilience indicators lower than the resilience threshold of 0.0100. This also indicates that choosing these points as distribution centers will face many risk factors. This discovery provides an important reference for resilience enhancement strategies in supply chain management, especially in the face of uncertain risks, on how to improve the risk-resistance capacity of cold chain supply chains through site selection and path optimization.

Through the above analysis, the site-path optimization model considering supply chain resilience constructed in this chapter has demonstrated remarkable scientificity and practicability in practical applications. The research results show that through reasonable site selection and route planning, the total transportation cost and total distribution time can be effectively reduced while ensuring the resilience of the supply chain. This research not only provides theoretical support for the management of the pharmaceutical supply chain, but also offers practical guidance for decision optimization in actual operations.

6. Conclusions and limitations

This study conducts an in-depth discussion on the site-routing optimization problem of the pharmaceutical supply chain, with a focus on considering the improvement effect of supply chain resilience on the transportation efficiency and reliability of vaccines. By constructing a dual-objective optimization model and combining it with the improved NSGA-II algorithm, the following main conclusions were obtained in this study:

1)Supply chain resilience plays a crucial role in vaccine transportation. By constructing a comprehensive resilience quantification model and subdividing resilience into levels such as production (vaccine production capacity ratio), economy (fiscal subsidies), and society (urban GDP), the impact of cold chain facilities, geographical location, and production capacity on supply chain resilience can be comprehensively depicted. Research has found that distribution centers with high resilience values such as Yueyang City and Shanwei City can better ensure the stable supply of vaccines due to their high level of cold chain infrastructure construction, financial subsidy intensity, and the transportation advantage of being close to large vaccine suppliers.

2) The dual-objective optimization model constructed in this paper can take into account both the total transportation cost and the total distribution time. Through the solution of the improved NSGA-II algorithm, the model generates multiple sets of Pareto optimal solutions, providing flexible site-path schemes for decision-makers. The experimental results show that the improved NSGA-II algorithm performs well in both the total transportation cost and the total distribution time in the scheme with Guangzhou City as the distribution center.

3) This paper, in combination with the actual data of the five provinces in South China, verifies the validity of the model and algorithm. By quantitatively analyzing the resilience and optimization plans of each urban distribution center, a basis has been provided for the decision-making of vaccine cold chain transportation. For example, the transportation time of the plan in Meizhou City is the best, and the transportation cost of the plan in Heyuan City is the best. Among them, the No. 5 plan in Heyuan City has a high resilience value and performs outstandingly in terms of cost and time, which has important reference value in actual decision-making.

Although certain achievements have been made in this study, the following limitations still exist:

Firstly, there are errors in some key data (such as urban demand and fiscal subsidies), and the research assumes that the demand and supply capacity of each city remain unchanged, which cannot reflect the changes brought about by seasonal fluctuations, policy adjustments or unexpected events, and has a certain impact on the accuracy and usability of the model. To simplify the problem, the model takes the sufficiency of vehicles and the stability of the transportation process as prerequisites, and does not consider the influence of traffic congestion, bad weather and unexpected situations on the transportation plan, resulting in the obtained scheme not being completely consistent with the actual situation. Secondly, the assessment of supply chain resilience is mainly based on physical indicators such as cold chain facilities and financial support, without incorporating socio-economic factors such as public trust and government emergency response. The evaluation perspective is relatively single. Furthermore, although the improved NSGA-II algorithm performs well in small-scale examples, there are still bottlenecks in convergence speed and computational efficiency for high-dimensional, multi-objective, and larger-scale problems. Furthermore, this study focuses on the distribution optimization of a single region and does not consider resource sharing and collaborative scheduling among different regions. Overall, data uncertainty, simplified assumptions, algorithm efficiency, evaluation dimensions and insufficient regional collaboration are the main limitations of this study.

In response to these deficiencies, future research can start from several aspects such as data dynamicization, model expansion, algorithm improvement and regional collaboration: Utilize real-time monitoring and big data analysis technologies (such as the LSTM time series model) to dynamically collect and predict key indicators to get rid of static assumptions; Further incorporate practical factors such as vehicle scheduling, resource constraints and traffic flow into the model, and integrate multi-level indicators such as physical, economic, policy and social trust into the resilience assessment framework; Combining deep reinforcement learning and federated learning, develop efficient parallel computing and intelligent optimization methods to enhance the global search and convergence performance of the improved NSGA-II on large-scale high-dimensional problems; Meanwhile, a cross-regional scheduling mechanism featuring information transparency and resource sharing is constructed through means such as blockchain to enhance the adaptability and resilience of the entire supply chain.

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