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INTEGRATING THE TRIPLE BOTTOM LINE OF SUSTAINABILITY, RESILIENCE STRATEGIES, AND PRODUCT PERISHABILITY CONSIDERATION TO DESIGN A PHARMACEUTICAL SUPPLY CHAIN NETWORK: A COVID-19 CASE STUDY

Alireza Roshani, Mohammad Reza Gholamian* and Mahsa Arabi

Abstract. This paper aims to design a resilient and sustainable pharmaceutical supply chain network under the perishability of medicine in which a multi-objective nonlinear mathematical model is formulated. To this end, four objective functions seek to minimize total cost, maximize the social indicators, minimize CO_2 emission and minimize de-resilience measures. Moreover, the three main categories of resilience strategies are integrated to mitigate the severe impacts of disruption. In order to solve the model, lexicographic goal programming is applied for small-scale problems, and NSGA-II is utilized for large-scale problems. The applicability of the proposed model is demonstrated by implementing it in a real case study during the COVID-19 situation. Also, a set of sensitivity analyses is conducted to validate the model and show the behavior of the objective functions. The results reveal the superiority of the resilient model with integrated strategies. Eventually, the Pareto front solutions are provided to quantify the trade-offs in satisfying the conflicting objective functions.

Mathematics Subject Classification. 90B06, 90B50, 90B80, 90B90, 90C11, 90C29, 68W50.

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1. Introduction

Supply Chains have encountered enormous challenges due to disease outbreaks in recent years. Between 2011 and 2018, the World Health Organization (WHO) tracked 1483 epidemic events in 172 countries. According to the Global Preparedness Monitoring Board (GPMB) reports published in 2019, loss cost from the economic and social impact of some past epidemics is estimated at more than $150 billion (*i.e.*, 2003 SARS, 2009 H1N1 influenza, and 2014 West Africa Ebola outbreak). Further, the COVID-19 pandemic has had even more severe impacts than previous ones. Although COVID-19 vaccination rates have been picked up around the world, COVID-19 immunity is currently impossible [1]. Therefore, the availability of medicines during the COVID-19 pandemic is always an essential need. In this regard, optimization techniques can be implemented beneficially to ensure the continuous flow of pharmaceutical supplies for infected people.

Keywords. Pharmaceutical supply chain, supply chain resilience, sustainable development, disruption risk, perishability, COVID-19.

School of Industrial Engineering, Iran University of Science and Technology (IUST), Narmak, Tehran, Iran.
*Corresponding author: gholamian@iust.ac.ir

One of the main COVID-19 issues that threaten the entire supply chain network is disruption by executing transport restrictions, shutting down manufacturing centers, closing borders, and the unavailability of raw materials [2]. Also, unpredictable dramatic growth in COVID-19 cases in a region leads to a shortage of medicine by increasing demand. Thus, adopting resilience strategies in the designing process of the Pharmaceutical Supply Chain (PSC) to avoid shortages and disruption is all the more crucial. Notably, the resilience of the supply chain is described as the ability of a supply chain to absorb disturbances and return to its initial state or move to a more desirable state after disruptions occur [3]. On the other hand, the environmental contamination caused by pharmaceutical waste and the social impact of COVID-19, as well as growing environmental and social concerns, force enterprises to consider sustainability as a crucial feature in designing and planning their supply chains. Still, another challenging issue in PSCs is drug perishability. Perishability consideration not only lowers the mortality rate during COVID-19 due to decreasing ineffectiveness but also avoids financial loss through expired medicines [4, 6].

Pharmaceutical industries in Iran were highly affected by the COVID-19 pandemic, which further limited access to essential medicines due to the sanction and import difficulties. In addition to the lockdowns, PSC has been impacted by distribution challenges resulting from transportation restrictions. Besides, Iranian manufacturers are currently struggling with serious issues such as limited production capacity and old technology levels. As a result, the vulnerability of the PSC to disruption, especially in manufacturers, leads to shortages of crucial medicines, and consequently, it works at the expense of human deaths. Hence, the potential for any disruptive events in the PSC network has attracted the government's attention.

To address these complex challenges, this paper presents a multi-objective mixed-integer nonlinear programming (MINLP) model designed to enhance the resilience and sustainability of the PSC while accounting for the perishability of drugs. By leveraging advanced mathematical techniques, this model optimizes the distribution and storage of pharmaceuticals, ensuring that medicines remain effective and reach those in need without unnecessary delay or waste. The model incorporates resilience strategies, sustainability considerations, and perishability into the network design, aiming to minimize total network costs and environmental impacts of CO_2 emissions while maximizing social indicators. This approach is crucial for managing the PSC more effectively amidst the disruptions caused by the COVID-19 pandemic and other similar crises.

To address these objectives, the following research questions are formulated:

– How can the integration of sustainability, resilience strategies, and product perishability be effectively incorporated into the design of a PSC network?
– What are the impacts of different resilience strategies on the performance and robustness of the PSC during disruptions?
– How does drug perishability influence the cost, environmental impact, and social outcomes within the PSC network?
– What are the trade-offs between minimizing costs, reducing CO_2 emissions, maximizing social indicators, and enhancing resilience in the PSC?
– What insights can be drawn from applying the proposed model to a real-world case study during the COVID-19 pandemic?

Finally, the main research purposes of this paper contributed to the literature are summarized as follows:

– Considering the triple bottom line (TBL) of sustainability along with resilience and drug perishability in a PSC network design.
– Integrating the three main categories of resilience strategies (see Sect. 2) and using them as optimization tools.
– Applying Lexicographic Goal Programming to solve the multi-objective model.
– Using NSGA-II in order to solve large-sized instances efficiently.
– Implement real-world data on COVID-19 outbreaks in the proposed model.

The rest of this paper is organized as follows. In Section 2, the literature review and relevant research in this field are discussed. Section 3 describes the problem definition of the resilient-sustainable PSC network during

COVID-19. In Section 4, the solution approaches are also dedicated. The validation, real-world case study, sensitivity analyses, and final results are presented in Section 5. Eventually, Section 6 contains the conclusion and directions for future work.

2. Literature review

The relevant research in the context of PSC can be classified into four main categories, namely (1) sustainable network design, (2) resilient supply chain, (3) integration of sustainability and resilience in supply chain network design (SCND) problems, and (4) supply chain considering product's perishability.

In the case of sustainability in SCND problems, Zhalechian *et al.* [7] proposed a sustainable Location-routeing-inventory problem that considers the environmental issues of GHG emissions and energy consumption and the social impacts of employment rate and economic development. Sharafati *et al.* [8] introduced a bi-objective non-linear programming model for sustainable SCND, aiming to maximize profits and address social responsibility and regional development. They used AHP to score and rank potential manufacturers based on work conditions and consumer issues. If environmental impacts exceed permissible values, manufacturers must repair and renovate. Mohammadian-Behbahani *et al.* [9] proposed a multi-objective stochastic programming model for blood SCND considering the social aspect of sustainability that seeks to minimize total cost and delivery time along with maximizing two indicators of consumer's health and the rate of regular blood donors. They also solved and evaluated their model by using robust optimization and conducting a case study of the Tehran Blood Transfusion Network. Jouzdani and Govindan [10] also presented a supply chain network for perishable dairy products, in which TBL of sustainability and perishability of products are considered. They applied some Sustainable Development Goals (SDGs) to their problem. The results of their case study indicate that decision-makers can obtain environmental and social benefits without compromising the economic aspect. Babaee Tirkolaee *et al.* [11] developed a mathematical model for a sustainable "face mask" closed-loop supply chain during COVID-19, focusing on minimizing total cost, pollution from transportation and operations, and human risk by reducing facilities in densely populated areas with high COVID-19 contamination risk. Azani *et al.* [12] presented a scenario-based bi-objective optimization model for a sustainable food supply chain during the COVID-19 pandemic, utilizing Food Hubs (FHs) to connect consumers to production sites efficiently. The model addresses cost reduction and environmental impact minimization, solving small and medium-sized problems with GAMS software and larger problems with a genetic algorithm. A real case study from Iran validates the model, demonstrating its feasibility and efficiency. Lotfi *et al.* [13] proposed a multi-objective optimization model for designing a closed-loop sustainable pharmaceutical supply chain network, incorporating recycling and sustainability considerations. The model utilizes the Analytical Hierarchy Process (AHP) for selecting green manufacturers and a linearized multi-objective nonlinear mathematical approach solved *via* the LP metric method in GAMS.

Amongst the relevant research works in the field of resiliency, Torabi *et al.* [14] developed a bi-objective two-stage stochastic model to build a resilient supply base for the global supply chain under operational and disruption risks. The model employed several resilient strategies, including pre-positioning emergency inventory, fortifying suppliers, contracting with backup suppliers, and suppliers' business continuity plans. Finally, numerical results indicated the significant impact of considering disturbances on the selected supply bases. Sabouhi *et al.* [15] presented an integrated PSC, including suppliers and manufacturers, in which manufacturers get raw materials from suppliers to manufacture the final product. In the first step, a fuzzy data envelopment analysis (DEA) model calculates the efficiency of potential suppliers. In the next step, a two-stage stochastic model selects and divides suppliers into two categories. Suppliers with no strategy are classified in the first category, while in the second category, suppliers have proactive plans to deal with disruptive events. Diabat *et al.* [16] presented a bi-objective robust optimization model to design a supply chain network considering the perishability of blood. The objective function aims to minimize the delivery time of blood's sub-products to demand points due to disruptions. In addition, they incorporate contracting with a backup facilities strategy to increase the resiliency of the network. Gholami-Zanjani *et al.* [17] proposed a two-stage stochastic programming model to design a resilient food supply chain under epidemic disruptions and demand uncertainty. Their research considers four resilience strategies: multiple sourcing, fortification/protection, backup facilities and capacity expansion. Rajabi *et al.* [18] developed a bi-objective mathematical model to design and optimize a pharmaceutical supply chain network under COVID-19 disruptions. The model, validated in Mashhad, Iran, aims to minimize economic costs and shortages by incorporating temporary distribution points and backup inventory. Additionally, they appended the particular characteristics of the food supply chain to the model, such as the perishability of the products and discount prices. Also, other numerous studies have taken the resiliency of networks into account (*e.g.*, [19–27]).

Given the increasing frequency of disruptions facing organizations and their inevitable impacts on supply chain sustainability performance, examining the supply chain without considering the interactions of both sustainability and resilience on the network is an unrealistic assumption [19]. To this end, many researchers have recently attempted to integrate sustainability and resiliency into their model [28]. Meanwhile, Zahiri *et al.* [29] proposed a novel linear mathematical model for resilient and sustainable PSC. More precisely, they utilized sustainability and resiliency measures as an optimization tool to tradeoff between them. Defining fuzzy possibilistic-stochastic programming to overcome the uncertainty of parameters and proposing a new evolutionary method to solve large-size problems have been the other contributions of their work. Jabbarzadeh *et al.* [30] developed a hybrid approach to design a sustainable supply chain network that considers resilient strategies in two phases. In the first phase, the sustainability performance of suppliers is assessed by the fuzzy c-means clustering method. In the next phase, a stochastic bi-objective model enhances the network's resilience using sustainability scores as input parameters. They also investigated their proposed approach in a real case study, and the results show the impact of joint consideration of resilience and sustainability on sourcing decisions and significant cost reduction. Yavari and Zaker [31] presented an integrated two-layer model that seeks to increase resilience in a green closed-loop supply chain of perishable products by designing a power distribution and transmission network. Haeri *et al.* [32] presented a multi-objective integrated resilient-efficient model for a blood SCND under uncertainty that objective function optimizes efficiency, total network cost, and resiliency of the network simultaneously. To deal with the uncertainty, they utilized a stochastic–robust formulation and motivational factors to increase blood donation to avoid shortage. Vali-Siar and Roghanian [33] developed resilient and sustainable closed-loop SCND problems under uncertainty and consideration of the COVID-19 situation. Three aspects of sustainability and the three most used resilience strategies are considered in their model. Foroozesh *et al.* [34] designed a green resilient supply chain network for perishable products, addressing route risk and horizontal collaboration under robust interval-valued type 2 fuzzy uncertainty. The study is developed in the form of multi-objective mixed integer linear programming model and validated in the food industry, with the aim of disruption impacts and CO_2 emissions.

Several studies have applied the perishability consideration to the SCND problem. In this regard, Rezaei-Malek *et al.* [35] proposed a hybrid location-allocation model to find the best ordering policy for renewing perishable products in the relief supply chain network. Also, they utilized a robust scenario-based stochastic approach due to the uncertainty of the problem. Their proposed model seeks to simultaneously minimize two objectives, (1) weighted average of response time and (2) total pre-disaster costs and penalties for unsatisfied demand and perished products at the post-disaster phase. Samani *et al.* [36] presented a novel mathematical model under both operational and disruption risks in which the diversity and perishability of blood products are considered. Further, they used a hybrid two-phase approach in which the first phase proposes an integration of Fuzzy AHP and grey rational analysis (GRA) technique to mitigate disruption risk. In the second phase, the model reduces operational risk by incorporating fuzzy-robust programming. Also, Akbarpour *et al.* [37] presented a robust pharmaceutical relief network under demand uncertainty and perishability of products consisting of suppliers and warehouses as pre-disaster nodes, and mobile pharmacies, hospitals, and affected areas as post-disaster nodes. To reduce the perished items, they provided a contractual framework between suppliers and the health organizations, in which suppliers commit to receiving the returned products when a specified time remains to the expiration date. Abbasi *et al.* [38] developed a bi-objective MINLP model for 3PL supply chain network design, focusing on cost and time minimization while managing disruption risks and product perishability. The model, validated through a pharmaceutical distribution case study in Iran, effectively optimizes hub and distribution center locations and fortifications. Hashemi-Amiri *et al.* [39] proposed a multi-objective mathematical model for designing a perishable food supply chain network that involves three stage decisions: supplier selection, production scheduling, and product distribution. Their model tries to minimize deterioration in the quality of the perishable product in the scheduling stage; hence, the fresh product reaches the retailer in the distribution stage. Shekoohi Tolgari and Zarrinpoor [40] presented a robust reverse PSC design model that addresses perishability and sustainable development goals. The model incorporates economic, social, and environmental objectives, utilizing a fuzzy best-worst method to weight the elements and a robust optimization approach to handle uncertainties. Numerical evidence from a practical case demonstrates the model's efficacy and validity, highlighting its potential to guide managerial and operational decisions in PSCs.

As stated earlier, several strategies are utilized to enhance supply chain resilience. Meanwhile, Sabouhi *et al.* [15] classified the most common of them in their paper. Moreover, for the first time, Zahiri *et al.* [29] incorporated node criticality and customer de-service level as two measures of resilience. Node criticality strategy seeks to minimize the number of critical nodes considered if the total flow of inputs and outputs exceeds a prespecified threshold. Customer de-service level strategy also tries to avoid demand shortage by minimizing the maximum unsatisfied demand. Additionally, a few researchers, such as Mari *et al.* [4], Dutta and Shrivastava [41] and Mousavi Ahranjan *et al.* [42], used a resilience measure called Expected Disruption Cost (EDC) calculated by expected losses incurred due to network disruption. Table 1 demonstrates some published papers that applied resilience measures/strategies to their model. Accordingly, the common resilience strategies can be summarized and divided into the following three categories:

– Supply and demand management strategies; Include multiple sourcing, contracting with backup facilities, fortification/protection of facilities, and customer de-service level.
– Network complexity management strategies include managing node criticality and managing node and flow complexity.
– Inventory management strategies; Include pre-positioning emergency inventory and capacity expansion.

As illustrated in Table 2, the simultaneous integration of sustainability, resilience, and product perishability has not been thoroughly investigated in existing researches. Specifically to the best of our knowledge, no prior studies have comprehensively addressed the Triple Bottom Line (TBL) – encompassing economic, environmental, and social dimensions – while also considering drug perishability. Additionally, Table 1 underscores a notable research gap in resilient models, particularly the absence of a unified approach that incorporates all three primary categories of resilience strategies. This study uniquely fills this gap by being the first to integrate these elements into a sustainable-resilient supply chain network design.

To address these identified gaps, this study endeavors to integrate the TBL of sustainability and resilience within a pharmaceutical supply chain (PSC), explicitly considering the perishability of drugs. This approach offers several advantages over previous studies:

– Comprehensive approach: by integrating TBL principles and perishability considerations, the model offers a holistic perspective on sustainability and resilience within the PSC.
– Addressing research gaps: the study directly tackles the identified gaps in the literature, contributing to a more robust understanding of sustainable and resilient PSCs.
– Real-world relevance: the proposed model is grounded in real-world data on COVID-19 outbreaks, providing a more practical and applicable framework.

3. Problem definition

In this study, a multi-objective nonlinear programming model is formulated to design a resilient and sustainable PSC network under the drug's perishability. As depicted in Figure 1, the proposed PSC network contains manufacturing centers (MCs), main distribution centers (DCs), local DCs, disposal centers (DSCs), and demand points. First, pharmaceutical products are consistently produced with different production and technology levels in MCs. The occurrence of any disruptive event leads technologies to become out of service. In this situation,

TABLE 1. Measures/strategies in resilient SCND literature.

		Authors (year)																				
		Mari *et al.* [4]	Torabi *et al.* [14]	Fahimnia and Jabbarzade [19]	Hasani and Khosrojerdi [20]	Khalili *et al.* [21]	Lücker and Seifert [22]	Namdar *et al.* [23]	Rezapour *et al.* [24]	Zahiri *et al.* [29]	Ghavamifar *et al.* [25]	Jabbarzadeh *et al.* [30]	Sabouhi *et al.* [15]	Diabat *et al.* [16]	Dutta and Shrivastava [41]	Haeri *et al.* [32]	Mousavi *et al.* [42]	Tucker *et al.* [26]	Gholami-Zanjani [17]	Vali-Siar and Roghanian [33]	Arabi and Gholamian [27]	This research
(I)	Multiple sourcing/assignment		✓	✓	✓		✓	✓	✓	✓		✓	✓						✓	✓	✓	✓
	Contracting with backup facilities		✓					✓				✓		✓					✓			
	Fortification/Protection of facilities				✓								✓						✓	✓		✓
	Customer de-service level									✓	✓					✓						✓
(II)	Capacity expansion					✓	✓		✓			✓						✓	✓	✓		
	Pre-positioning emergency inventory		✓		✓	✓			✓				✓					✓				✓
(III)	Managing flow/node complexity									✓						✓						✓
	Managing node criticality									✓						✓						✓
	Developing business continuity plans		✓															✓				
	Expected disruption cost (EDC)	✓													✓		✓					

TABLE 2. Reviewed papers.

		Performance measures										Time period		Solution method		Objective function		Uncertainty method			
			Sustainability			Risk															
	Authors	Cost/profit	Economic	Environmental	Social	Disruption	Operational	Resiliency	Perishability	Demand	Model type*	Single period	Multi period	Exact	(Meta) heuristic	Single objective	Multi objective	Stochastic	Fuzzy	Robust	Case study/application
1	Torabi *et al.* [14]	✓				✓		✓			TSSP		✓		✓		✓	✓			–
2	Fahimnia and Jabbarzade [19]	✓	✓	✓	✓	✓		✓			TSSP		✓	✓			✓	✓	✓		Garment Industry
3	Rezaei-Malek *et al.* [35]	✓				✓			✓		MILP		✓	✓			✓	✓		✓	Relief commodities
4	Zhalechian *et al.* [7]	✓	✓	✓	✓						MINLP		✓		✓		✓	✓			LCD and LED TV
5	Zahiri *et al.* [29]	✓	✓	✓	✓	✓		✓			MILP		✓	✓	✓		✓		✓		Pharmaceutical
6	Jabbarzadeh *et al.* [30]	✓	✓	✓	✓	✓		✓			TSSP		✓	✓			✓	✓			Plastic pipe industry
7	Sabouhi *et al.* [15]	✓				✓		✓			TSPSP	✓		✓		✓		✓	✓		Pharmaceutical
8	Diabat *et al.* [16]	✓				✓		✓	✓		TSSP		✓	✓			✓	✓		✓	Blood Transfusion
9	Mohammadian-Behbahani *et al.* [9]	✓	✓		✓						MILP		✓	✓			✓	✓		✓	Blood Transfusion
10	Roshan *et al.* [5]	✓	✓		✓	✓				✓	MINLP		✓	✓			✓		✓		Pharmaceutical
11	Sherafati *et al.* [8]	✓	✓	✓	✓						MILP		✓	✓			✓			✓	Cable industry
12	Yavari and Zaker [31]	✓	✓	✓		✓		✓	✓		MILP		✓	✓			✓			✓	Dairy industry
13	Akbarpour *et al.* [37]	✓							✓	✓	TSSP		✓	✓			✓	✓		✓	Pharmaceutical
14	Haeri *et al.* [32]	✓	✓		✓	✓		✓			MILP	✓		✓			✓			✓	Blood Transfusion
15	Jouzdani and Govindan [10]	✓	✓	✓	✓				✓		GP		✓	✓			✓	✓			Dairy industry
16	Gholami-Zanjani *et al.* [17]	✓				✓		✓			TSSP		✓	✓		✓		✓			–
17	Babaee Tirkolaee *et al.* [11]	✓	✓	✓	✓						MILP		✓		✓		✓				Mask distribution, COVID-19
18	Vali-Siar and Roghanian [33]	✓	✓	✓	✓	✓		✓		✓	MILP		✓	✓	✓		✓	✓		✓	Tire industry, COVID-19
19	Foroozesh *et al.* [34]			✓		✓		✓	✓		MILP		✓	✓			✓		✓	✓	Food industry
20	Hashemi-Amiri *et al.* [39]	✓							✓		GP, MILP		✓	✓			✓			✓	Poultry processing, COVID-19
21	Lotfi *et al.* [13]	✓	✓	✓					✓		MINLP, AHP		✓	✓			✓				Pharmaceutical
22	Rajabi *et al.* [18]	✓	✓			✓		✓			MILP		✓	✓			✓				Pharmaceutical, COVID-19
23	Shekoohi Tolgari and Zarrinpoor [40]	✓	✓	✓	✓				✓		BWM		✓	✓			✓		✓	✓	Pharmaceutical
24	This Research	✓	✓	✓	✓	✓		✓	✓	✓	LGP, MINLP		✓	✓	✓		✓				Pharmaceutical, COVID-19

Notes. (*)The abbreviation of model types is defined as follows. BWM: Best-Worst Method, S: Simulation, TSSP: Two-Stage Stochastic Programing, MSSP: Multi-Stage Stochastic Programing, MILP: Mixed Integer Linear Programing, MINLP: Mixed Integer Non-Linear programming, SP: Stochastic Programming, MIP: Mixed Integer Programing, GP: Goal Programming, LGP: Lexicographic Goal Programming.

the reassignment policy is employed to avoid decreasing production by reallocating failed technologies to non-failable ones. Then, the packed drugs are transported to main and local DCs for stocking and further sent to demand points to be met if faced with a demand. It is also considered that drugs in each MC, main DC, and local DC are perishable and have a certain shelf life. Therefore, the perished products are shipped to DSCs in each period because of their hazards.

Sustainability and resiliency are taken into account as the two main keys of the proposed PSC network. All three aspects of sustainability are considered in this paper. The economic aspect includes the network's total cost, the environmental aspect focuses on CO_2 emission, and the social aspect includes job opportunities, unemployment rate, and regional development rate. Furthermore, three main categories of strategies/measures as optimization tools are integrated to make the whole network more resilient toward any disruption. In this regard, (I) supply and demand management strategies contain multiple sourcing and customer de-service level, (II) network complexity management strategies include managing node criticality, managing node and flow complexity [29, 32, 43], and finally, pre-positioning emergency inventory is used as (III) inventory management strategy [14]. More details and mathematical formulations for these strategies/measures are provided in Section 3.2.2.

Notably, the assumptions have been considered as follows:

- The candidate locations of MCs, main and local DCs, and DSCs are pre-determined.
- There are different transportation modes for shipping the products between nodes.
- All facilities have limited capacity.
- There are different sets of production technologies in MCs, classified into old and new ones.
- The sale and purchase of technologies are allowable for manufacturers.
- A reliable technology level called the non-failable technology would be eventually assigned if all previous technology levels had failed.
- There is a specified strategic stock over each period and product.
- In each period, a percentage of pharmaceutical products perished in MCs and DCs and then shipped to the DSCs.
- DSCs have a specified upper and lower bound for disposal capacity at the end of periods.

3.1. Notations

The following indices, parameters, and variables will be used in the mathematical model:

Sets

I	Set of manufacturing centers indexed by $i \in \{1, 2, \ldots, I\} = I$
J	Set of main distribution centers indexed by $j \in \{1, 2, \ldots, J\} = J$
K	Set of local distribution centers indexed by $k \in \{1, 2, \ldots, K\} = K$
D	Set of disposal centers indexed by $d \in \{1, 2, \ldots, D\} = D$
H	Set of demand points indexed by $h \in \{1, 2, \ldots, H\} = H$
A	Set of allocated production levels indexed by $a, a' \in \{1, 2, \ldots, A\} = A$
L	Set of technology levels indexed by $l, l' \in \{1, 2, \ldots, L, L+1\} = L$
$L+1$	Set of non-failable technology levels indexed by $l+1 \in \{L+1\} = L+1$ (a singleton set) $\subset L$
O	Set of old technology levels indexed by $o \in \{1, 2, \ldots, O\} = O \subset L$
N	Set of new technology levels indexed by $n \in \{O+1, O+2, \ldots, L\} = N \subset L$

M	Set of transport types indexed by $m \in \{1,2,\ldots,M\} = M$
P	Set of products indexed by $p \in \{1,2,\ldots,P\} = P$
T	Set of time periods indexed by $t \in \{1,2,\ldots,T\} = T$

Parameters

ec_i	The cost of establishing MC i
ec'_j	The cost of establishing main DC j
ec''_k	The cost of establishing local DC k
ec'''_d	The cost of establishing DSC d
pc_{pil}	Cost of producing product p by MC i using technology l
tc_{ijm}	The transportation cost of products between node i and j with transport type m
tc'_{ikm}	The transportation cost of products between node i and k with transport type m
tc''_{jkm}	The transportation cost of products between node j and k with transport type m
tc'''_{khm}	The transportation cost of products between node k and h with transport type m
$tc^{(4)}_{idm}$	The transportation cost of products between node i and d with transport type m
$tc^{(5)}_{jdm}$	The transportation cost of products between node j and d with transport type m
$tc^{(6)}_{kdm}$	The transportation cost of products between node k and d with transport type m
cd_{dp}	The operation cost of product p in DSC d
cap_i	The capacity of storage in MC i
${cap'}_j$	The capacity of storage in main DC j
${cap''}_k$	The capacity of storage in local DC k
${cap'''}_d$	The capacity of storage in DSC d
λ^t_p	Percentage of product p that is perished in time period t in the MC
${\lambda'}^t_p$	Percentage of product p that is perished in time period t in the main DC
${\lambda''}^t_p$	Percentage of product p that is perished in time period t in the local DC
θ_{pil}	Producing capacity of product p by MC i using technology l
δ_d	Minimum disposal capacity in DSC d
Δ_d	Maximum disposal capacity in DSC d
hc_{pi}	The inventory holding cost for product p in MC i
hc'_{pj}	The cost of inventory holding for product p in main DC j
hc''_{pk}	The cost of inventory holding for product p in local DC k
hc'''_{dp}	The cost of inventory holding for product p in DSC d

$Emghc'_{pj}$	The cost of inventory holding for the pre-position emergency inventory of product p in main DC j
$Emghc''_{pk}$	The cost of inventory holding for the pre-position emergency inventory of product p in local DC k
cc_i	The price of selling carbon credit by MC i
cc'_i	The price of purchasing carbon credit by MC i
cp_{il}	The purchasing cost of new technology l by MC i
cs_{il}	The selling cost of technology l by MC i
jo_i	Number of jobs created by establishing MC i
jo'_j	Number of jobs created by establishing main DC j
jo''_k	Number of jobs created by establishing local DC k
jo'''_d	Number of jobs created by establishing DSC d
unr_i	The unemployment rate of the MC i location
unr'_j	The unemployment rate of the main DC j location
unr''_k	The unemployment rate of local DC k location
unr'''_d	The unemployment rate of DSCd location
$re\nu_i$	The GDP share of MC i location
$re\nu'_j$	The GDP share of the main DC j location
$re\nu''_k$	The GDP share of local DC k location
$re\nu'''_d$	The GDP share of DSC d
rdf_i	The regional development factor of MC i location
rdf'_j	The regional development factor of the main DCj location
rdf''_k	The regional development factor of local DC k location
rdf'''_d	The regional development factor of DSC d
set^t_{il}	CO_2 emission of setting up technology l in time period t by MC i
$pef'^t_{pil}(.)$	CO_2 emission of producing product p with technology l in time period t by MC i
$de''^t_{pd}(.)$	CO_2 emission of disposal operation for product p in DSC d in time period t
ti_{ijm}	CO_2 emission from transporting each product between node i and j using transport type m
ti'_{ikm}	CO_2 emission from transporting each product between node i and k using transport type m
ti''_{jkm}	CO_2 emission from transporting each product between node j and k using transport type m
ti'''_{khm}	CO_2 emission from transporting each product between node k and h using transport type m
$ti^{(4)}_{idm}$	CO_2 emission from transporting each product between node i and d using transport type m

$ti^{(5)}_{jdm}$	CO_2 emission from transporting each product between node j and d using transport type m
$ti^{(6)}_{kdm}$	CO_2 emission from transporting each product between node k and d using transport type m
α	Node criticality coefficient of MCs
α'	Node criticality coefficient of main DCs
α''	Node criticality coefficient of local DCs
α'''	Node criticality coefficient of DSCs
β	Flow complexity coefficient between MCs and main DCs
β'	Flow complexity coefficient between MCs and local DCs
β''	Flow complexity coefficient between the main and local DCs
β'''	Flow complexity coefficient between the local DCs and demand points
$\beta^{(4)}$	Flow complexity coefficient between MCs and DSCs
$\beta^{(5)}$	Flow complexity coefficient between main DCs and DCSs
$\beta^{(6)}$	Flow complexity coefficient between local DCs and DSCs
γ	Node complexity coefficient of MCs
γ'	Node complexity coefficient of main DCs
γ''	Node complexity coefficient of local DCs
γ'''	Node complexity coefficient of DSCs
ξ	The coefficient of demand dissatisfaction level
τ	The coefficient of producing with old technologies
ϑ'_{pj}	The coefficient for the pre-position emergency inventory of product p in main DC j
ϑ''_{pk}	The coefficient for the pre-position emergency inventory of product p in local DC k
D^t_{ph}	Demand for product p in time period t and demand point h
SS^t_p	Strategic stock for product p in time period t
pd^t_{il}	Probability of disruption in MC i in time period t using technology l
ae^t_i	Allowed CO_2 emission for MC i in time period t
ae'^t_d	Allowed CO_2 emission for DSC d in time period t
U^t_i	The threshold of the criticality for node i in time period t
U'^t_j	The threshold of the criticality for node j in time period t
U''^t_k	The threshold of the criticality for node k in time period t
U'''^t_d	The threshold of the criticality for node d in time period t

$ncc_t^{-\max}$	The maximum value of carbon credit could be sold in MC i
$ncc_i^{+\max}$	The maximum value of carbon credit could be bought in MC i
M	A sufficiently large positive constant

Variables

y_i	A binary variable, equal to 1 if an MC is established in region i; 0 otherwise
w_j	A binary variable, equal to 1 if a main DC is established in region j; 0 otherwise
z_k	A binary variable, equal to 1 if a local DC is established in region k; 0 otherwise
u_d	A binary variable, equal to 1 if a DSC is established in region d; 0 otherwise
y'_i	A binary variable, equal to 1 if MC i is a critical node; 0 otherwise
w'_j	A binary variable, equal to 1 if main DC j is a critical node; 0 otherwise
z'_k	A binary variable, equal to 1 if local DC k is a critical node; 0 otherwise
u'_d	A binary variable, equal to 1 if DSC d is a critical node; 0 otherwise
ν_{ij}^t	A binary variable, equal to 1 if node i is assigned to node j; 0 otherwise
$\nu_{ik}'^t$	A binary variable, equal to 1 if node i is assigned to node k; 0 otherwise
$\nu_{jk}''^t$	A binary variable, equal to 1 if node j is assigned to node k; 0 otherwise
$\nu_{kh}'''^t$	A binary variable, equal to 1 if node k is assigned to node h; 0 otherwise
$\nu_{id}^{(4)t}$	A binary variable, equal to 1 if node i is assigned to node d; 0 otherwise
$\nu_{jd}^{(5)t}$	A binary variable, equal to 1 if node j is assigned to node d; 0 otherwise
$\nu_{kd}^{(6)t}$	A binary variable, equal to 1 if node k is assigned to node d; 0 otherwise
n_{pil}^{at}	A binary variable, equal to 1 if product p is produced with technology l at level a by MC i in time period t; 0 otherwise
tp_{il}^t	A binary variable, equal to 1 if new technology l is purchased in time period t by MC i; 0 otherwise
$tncc_{il}^t$	A binary variable, equal to 1 if technology is sold in time period t by MC i; 0 otherwise
In_{pi}^t	Inventory of product p in MC i and time period t
$In_{pj}'^t$	Inventory of product p in main DC j and time period t
$In_{pk}''^t$	Inventory of product p in local DC k and time period t
$In_d'''^t$	Inventory of product p in DSC d and time period t
$EmgIn'^t_{pj}$	Pre-position emergency inventory of product p in main DC j and time period t
$EmgIn''^t_{pk}$	Pre-position emergency inventory of product p in local DC k and time period t
qnt_{pil}^t	Quantity of product p produced with technology l by MC i in time period t
qnt'^t_{pd}	Quantity of perished product p disposed by DSC d in time period t
xp_{pijm}^t	The product p flow shipped between node i and j using transport type m in time period t

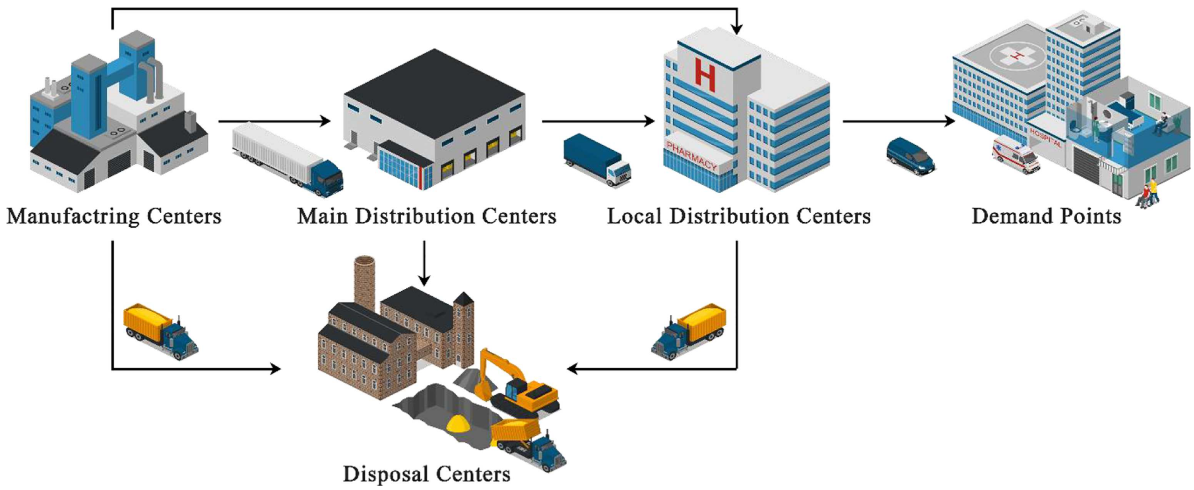


FIGURE 1. Schematic of the proposed PSC network.

xp'^{t}_{pikm}	The product p flow shipped between node i and k using transport type m in time period t
xp''^{t}_{pjkm}	The product p flow shipped between node j and k using transport type m in time period t
xp'''^{t}_{pkhm}	The product p flow shipped between node k and h using transport type m in time period t
$xp^{(4)t}_{pidm}$	The product p flow shipped between node i and d using transport type m in time period t
$xp^{(5)t}_{pjdm}$	The product p flow shipped between node j and d using transport type m in time period t
$xp^{(6)t}_{pkdm}$	The product p flow shipped between node k and d using transport type m in time period t
ncc_i^{-t}	The number of carbon credits sold in MC i and time period t
ncc_i^{+t}	The number of carbon credits bought in MC i and time period t
P^{at}_{pil}	Transitional probability of producing product p with technology l and production level a by MC i in time period t
ϕ	A variable for linearization of the customer de-service level equation

3.2. Mathematical model

In this section, a nonlinear mathematical model is provided to design the PSC network where the objective functions seek to achieve sustainability goals through minimizing the total cost, CO_2 emission, and maximizing social indicators, as well as resiliency goals by minimizing de-resilience measures.

3.2.1. TBL of sustainability (first to third objective functions)

Equation (1) shows the first objective function, including seven terms, minimizes the total cost of the PSC network. These terms are the establishment, production, disposal, shipment, inventory, selling and buying carbon credit, and production technology costs, respectively. The second objective function illustrated in equation (2) seeks to maximize total job opportunities created in regions with a high unemployment rate and low regional development rate. It is noteworthy to mention that the coefficients ω and ω' are related to job opportunities and the regional economic value, respectively, which are valued by the decision maker. Furthermore, the third objective function in equation (3) represents the environmental aspect that minimizes the total CO_2 emission with respect to production and disposal operation and vehicle transportation.

$$\begin{aligned}
\mathrm{Min}\, Z_1 = {} & \sum_{i\epsilon I} ec_i y_i + \sum_{j\epsilon J} ec'_j w_j + \sum_{k\epsilon K} ec''_k z_k + \sum_{d\epsilon D} ec'''_d u_d + \sum_{t\epsilon T}\sum_{p\epsilon P}\sum_{l\epsilon L}\sum_{i\epsilon I} (cq)_{pil} qnt^t_{pil} \\
& + \sum_{t\epsilon T}\sum_{p\epsilon P}\sum_{d\epsilon D} cd_{dp} qnt'^t_{dp} + \sum_{t\epsilon T}\sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{j\epsilon J}\sum_{i\epsilon I} tc_{ijm} xp^t_{pijm} + \sum_{t\epsilon T}\sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{k\epsilon K}\sum_{i\epsilon I} tc'_{ikm} xp'^t_{pikm} \\
& + \sum_{t\epsilon T}\sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{k\epsilon K}\sum_{j\epsilon J} tc''_{jkm} xp''^t_{pjkm} + \sum_{t\epsilon T}\sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{h\epsilon H}\sum_{k\epsilon K} tc'''_{khm} xp'''^t_{pkhm} \\
& + \sum_{t\epsilon T}\sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{h\epsilon H}\sum_{k\epsilon K} tc^{(4)}_{idm} xp^{(4)t}_{pidm} + \sum_{t\epsilon T}\sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{h\epsilon H}\sum_{k\epsilon K} tc^{(5)}_{jdm} xp^{(5)t}_{pjdm} \\
& + \sum_{t\epsilon T}\sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{h\epsilon H}\sum_{k\epsilon K} tc^{(6)}_{kdm} xp^{(6)t}_{pkdm} + \sum_{t\epsilon T}\sum_{p\epsilon P}\sum_{i\epsilon I} hc_{pi} In^t_{pi} + \sum_{t\epsilon T}\sum_{p\epsilon P}\sum_{j\epsilon J} hc'_{pj} I'^t_{pj} \\
& + \sum_{t\epsilon T}\sum_{p\epsilon P}\sum_{k\epsilon K} hc''_{pk} I''^t_{pk} + \sum_{t\epsilon T}\sum_{p\epsilon P}\sum_{d\epsilon D} hc'''_{dp} I'''^t_{dp} + \sum_{t\epsilon T}\sum_{p\epsilon P}\sum_{j\epsilon J} Emghc'_{pj} EmgIn'^t_{pj} \\
& + \sum_{t\epsilon T}\sum_{p\epsilon P}\sum_{k\epsilon K} Emghc''_{pk} EmgIn''^t_{pk} - \sum_{t\epsilon T}\sum_{i\epsilon I} cc_i ncc^{-t}_i + \sum_{t\epsilon T}\sum_{i\epsilon I} cc'_i ncc^{+t}_i \\
& - \sum_{t\epsilon T}\sum_{l\epsilon L}\sum_{i\epsilon I} cs_{il} tncc^t_{il} + \sum_{t\epsilon T}\sum_{l\epsilon L}\sum_{i\epsilon I} cp_{il} tp^t_{il}
\end{aligned} \tag{1}$$

$$\begin{aligned}
\mathrm{Max}\, Z_2 = {} & \omega\left(\sum_{i\epsilon I} jo_i unr_i y_i + \sum_{j\epsilon J} jo'_j unr'_j w_j + \sum_{k\epsilon K} jo''_k unr''_k z_k + \sum_{d\epsilon D} jo'''_d unr'''_d u_d\right) \\
& + \omega'\Bigg(\sum_{i\epsilon I} rev_i y_i (1 - rdf_i) + \sum_{j\epsilon J} rev'_j w_j (1 - rdf'_j) + \sum_{k\epsilon K} rev''_k z_k (1 - rdf''_k) \\
& + \sum_{d\epsilon D} rev'''_d u_d (1 - rdf'''_d)\Bigg)
\end{aligned} \tag{2}$$

$$\begin{aligned}
\mathrm{Min}\, Z_3 = {} & \sum_{t\epsilon T}\sum_{l\epsilon L}\sum_{i\epsilon I} set_{il} y_i + \sum_{t\epsilon T}\sum_{p\epsilon P}\sum_{l\epsilon L}\sum_{i\epsilon I} pef'^t_{pil}(qnt^t_{pil}) qnt^t_{pil} + \sum_{t\epsilon T}\sum_{p\epsilon P}\sum_{d\epsilon D} de''^t_{pd}(qnt'^t_{pd}) qnt'^t_{pd} \\
& + \sum_{t\epsilon T}\sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{j\epsilon J}\sum_{i\epsilon I} ti_{ijm} xp^t_{pijm} + \sum_{t\epsilon T}\sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{k\epsilon K}\sum_{i\epsilon I} ti'_{ikm} xp'^t_{pikm} \\
& + \sum_{t\epsilon T}\sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{k\epsilon I}\sum_{j\epsilon J} ti''_{jkm} xp''^t_{pjkm} + \sum_{t\epsilon T}\sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{h\epsilon H}\sum_{k\epsilon K} ti'''_{khm} xp'''^t_{pkhm} \\
& + \sum_{t\epsilon T}\sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{d\epsilon D}\sum_{i\epsilon I} ti^{(6)}_{kdm} xp^{(6)t}_{pkdm} + \sum_{t\epsilon T}\sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{d\epsilon D}\sum_{i\epsilon I} ti^{(4)}_{idm} xp^{(4)t}_{pidm} \\
& + \sum_{t\epsilon T}\sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{d\epsilon D}\sum_{i\epsilon J} ti^{(5)}_{jdm} xp^{(5)t}_{pjdm}.
\end{aligned} \tag{3}$$

3.2.2. Resilience strategies (terms of the fourth objective function)

As mentioned earlier, the three main categories of strategies have been integrated to enhance the network resilience level, and their mathematical formulations are provided here. Multiple sourcing, customer de-service level, node criticality, flow and node complexity as negative measures must be minimized in the model. At the same time, pre-position emergency inventory must be maximized by virtue of its positive impact on resiliency.

– **Multiple sourcing (multiple assignments)**

Most papers used this strategy in their resilient supply chain model in which the manufacturer can purchase raw materials from more than one supplier. In doing so, the supply chain network has become more resilient rather than the single sourcing strategy [20, 23, 30, 33]. Similarly, multiple technology assignment has been used instead of multiple supplier sourcing, where the manufacturers are allowed to sell and purchase different levels of technology in this research. These technologies are divided into old and new ones. Although it could be more costly to purchase new technologies, it is also more reliable. Additionally, a more reliable technology would be assigned to the production if the current technology has been disrupted. This procedure will be continued until the non-failable technology is assigned. Thus, any disruption couldn't stop the production in MCs. The model aims to minimize the total amount of drugs produced with the old technology ($\sum_{t,p,l\epsilon O,i} qnt^t_{pil}$).

– **Customer de-service level**

This measure calculates the unsatisfied demand of each product in demand points and time periods by minimizing the maximum difference between the amount of demand and the latest flow shipping to the demand point. The mathematical formulation of customer de-service level is provided below where ψ^t_{hp} is a weight factor.

$$\min \max_{p,h,t} \psi^t_{ph} \left(D^t_{ph} - \sum_{k\epsilon K} \sum_{m\epsilon M} xp'''^t_{pkhm} \right). \tag{4}$$

Linearization of the customer de-service level equation is defined using equations (5)–(7).

$$\min \phi \tag{5}$$

$$\phi \geq \sigma \left(D^t_{ph} - \sum_{k\epsilon K} \sum_{m\epsilon M} xp'''^t_{pkhm} \right), \tag{6}$$

$$\phi \geq 0. \tag{7}$$

– **Node criticality**

This measure indicates that if a node's total inputs and outputs flow exceed a prespecified threshold, it will be a critical node. Equations (8)–(11) calculate node criticality for MCs, main and local DCs, and DSCs, respectively [29]. It is noteworthy to mention that equations (8)–(11) are not considered model constraints and are given only to comprehend the node criticality. Moreover, the corresponding constraints are provided in equations (27)–(30).

$$y'_i = 1| \sum_{p\epsilon P} \sum_{l\epsilon L} qnt^t_{pil} + \sum_{j\epsilon J} \sum_{p\epsilon P} \sum_{m\epsilon M} xp^t_{pijm} + \sum_{m\epsilon M} \sum_{p\epsilon P} \sum_{k\epsilon K} xp'^t_{pikm} > U^t_i, \qquad \forall i, t \tag{8}$$

$$w'_j = 1| \sum_{m\epsilon M} \sum_{p\epsilon P} \sum_{i\epsilon I} xp^t_{pijm} + \sum_{m\epsilon M} \sum_{p\epsilon P} \sum_{k\epsilon K} xp''^t_{pjkm} > U'^t_j, \qquad \forall j, t \tag{9}$$

$$z'_k = 1| \sum_{m\epsilon M} \sum_{p\epsilon P} \sum_{i\epsilon I} xp'^t_{pikm} + \sum_{m\epsilon M} \sum_{p\epsilon P} \sum_{j\epsilon J} xp''^t_{pjkm} + \sum_{m\epsilon M} \sum_{p\epsilon P} \sum_{h\epsilon H} xp'''^t_{pkhm} > U''^t_k, \qquad \forall k, t \tag{10}$$

$$u'_d = 1| \sum_{m\epsilon M} \sum_{p\epsilon P} \sum_{i\epsilon I} xp^{(4)t}_{pidm} + \sum_{m\epsilon M} \sum_{p\epsilon P} \sum_{j\epsilon J} xp^{(5)t}_{pjdm} + \sum_{m\epsilon M} \sum_{p\epsilon P} \sum_{k\epsilon K} xp^{(6)t}_{pkdm} > U'''^t_d, \qquad \forall d, t. \tag{11}$$

– **Flow and node complexity**

Flow complexity ($\sum_{t,j,i} \nu^t_{ij} + \sum_{t,k,i} \nu'^t_{ik} + \ldots + \sum_{t,d,k} \nu^{(6)t}_{kd}$) calculates the total amount of flow interacted between nodes, and also, node complexity ($\sum_i y_i + \sum_j w_j + \sum_k z_k + \sum_d u_d$) shows the total number of active nodes. So, if the value of these two equations is high, the network has flow and/or node complexity. In other words, the flow complexity measure seeks to minimize the total number of corresponding links, and similarly, node complexity tries to minimize the total number of nodes.

– **Preposition emergency inventory**

Here, pre-positioning of emergency inventory in main and local DCs has been considered to increase the network resilience toward disruption occurrence. Although considering pre-position emergency inventory makes the whole PSC more resilient, it imposes the holding cost on the network. It is also assumed that the total amount of pre-position emergency inventory must be exceeded a specified strategic stock (see Eq. (19)). The total amount of pre-position emergency inventory is calculated by $\sum_{t,p,j} EmgIn_{pj}^{\prime t} + \sum_{t,p,k} EmgIn_{pk}^{\prime\prime t}$ and placed in both the cost objective function (*i.e.*, Eq. (1)) and objective function of resilience (*i.e.*, Eq. (12)) to make a tradeoff relation between them. Further, due to the positive impact of this measure on resiliency, it must be deducted from all other de-resilience measures.

Considering the aforementioned points, equation (12) represents the fourth objective function which aims to minimize the de-resilience measures.

$$\begin{aligned}\text{Min } Z_4 = {} & \sum_{t\epsilon T}\sum_{p\epsilon P}\sum_{o\epsilon O}\sum_{i\epsilon I}\tau\left(qnt_{iop}^{t}\right) + \xi\Phi + \sum_{i\epsilon I}\alpha y_i' + \sum_{j\epsilon J}\alpha' w_j' + \sum_{k\epsilon K}\alpha'' z_k' + \sum_{d\epsilon D}\alpha''' u_d' \\ & + \sum_{t\epsilon T}\sum_{j\epsilon J}\sum_{i\epsilon I}\beta\nu_{ij}^{t} + \sum_{t\epsilon T}\sum_{k\epsilon K}\sum_{i\epsilon I}\beta'\nu_{ik}^{\prime t} + \sum_{t\epsilon T}\sum_{k\epsilon K}\sum_{j\epsilon J}\beta''\nu_{jk}^{\prime\prime t} + \sum_{t\epsilon T}\sum_{h\epsilon H}\sum_{k\epsilon K}\beta'''\nu_{kh}^{\prime\prime\prime t} \\ & + \sum_{t\epsilon T}\sum_{d\epsilon D}\sum_{i\epsilon I}\beta^{(4)}\nu_{id}^{(4)t} + \sum_{t\epsilon T}\sum_{d\epsilon D}\sum_{j\epsilon J}\beta^{(5)}\nu_{jd}^{(5)t} + \sum_{t\epsilon T}\sum_{d\epsilon D}\sum_{k\epsilon K}\beta^{(6)}\nu_{kd}^{(6)t} + \sum_{i\epsilon I}\gamma w_i \\ & + \sum_{j\epsilon J}\gamma' y_j + \sum_{k\epsilon K}\gamma'' z_k + \sum_{d\epsilon D}\gamma''' u_d - \sum_{t\epsilon T}\sum_{p\epsilon P}\sum_{j\epsilon J}\vartheta_{pj}' EmgIn_{pj}^{\prime t} - \sum_{t\epsilon T}\sum_{p\epsilon P}\sum_{k\epsilon K}\vartheta EmgIn_{pk}^{\prime\prime t}. \end{aligned} \tag{12}$$

3.2.3. Constraints

In this section, the constraints of the proposed mathematical model are provided.

– **Inventory balance constraints**

Constraint (13) illustrates that the inventory balance of MCs (In_{pi}^{t}) is equal to a percentage of the previous period inventory perishes ($\left(1-\lambda_p^t\right)In_{pi}^{t-1}$), plus the produced product by MC i with all technology levels ($\sum_l qnt_{pil}^{t}$), subtracting the product flow from MC i to DCs j ($\sum_{m\epsilon M}\sum_{j\epsilon J} xp_{pijm}^{t}$) and local DCs k ($\sum_{m\epsilon M}\sum_{k\epsilon K} xp_{pikm}^{\prime t}$) in each period t. Similarly, constraints (14)–(16) show the inventory balance constraints of main DCs ($In_{pj}^{\prime t}$), local DCs ($In_{pk}^{\prime\prime t}$), and DSCs ($\sum_{p\epsilon P} In_{dp}^{\prime\prime\prime t}$) [44].

Furthermore, constraints (17) and (18) are balance constraints for pre-position emergency inventory in DCs. It's noteworthy that the initial inventory at the beginning of the period is set to zero.

$$In_{pi}^{t} = \left(1-\lambda_p^t\right)In_{pi}^{t-1} + \sum_{l} qnt_{pil}^{t} - \sum_{m\epsilon M}\sum_{j\epsilon J} xp_{pijm}^{t} - \sum_{m\epsilon M}\sum_{k\epsilon K} xp_{pikm}^{\prime t}, \qquad \forall i,p,t\geq 1 \tag{13}$$

$$In_{pj}^{\prime t} = \left(1-\lambda_p'\right)In_{pj}^{'t-1} + \sum_{m\epsilon M}\sum_{j\epsilon J} xp_{pijm}^{t} - \sum_{m\epsilon M}\sum_{k\epsilon K} xp_{pjkm}^{\prime\prime t}, \qquad \forall j,p,t\geq 1 \tag{14}$$

$$In_{pk}^{\prime\prime t} = \left(1-\lambda_p''\right)In_{pk}^{''t-1} + \sum_{m\epsilon M}\sum_{i\epsilon I} xp_{pikm}^{\prime t} + \sum_{m\epsilon M}\sum_{j\epsilon J} xp_{pjkm}^{\prime\prime t} - \sum_{m\epsilon M}\sum_{h\epsilon H} xp_{pkhm}^{\prime\prime\prime t}, \qquad \forall k,p,t\geq 1 \tag{15}$$

$$\begin{aligned}\sum_{p\epsilon P} In_{dp}^{\prime\prime\prime t} = {} & \sum_{p\epsilon P} In_{dp}^{'''t-1} - \sum_{p\epsilon P} qnt_{dp}^{\prime t} + \sum_{p\epsilon P}\sum_{m\epsilon M}\sum_{i\epsilon I} xp_{pidm}^{(4)t} + \sum_{p\epsilon P}\sum_{m\epsilon M}\sum_{j\epsilon J} xp_{pjdm}^{(5)t} \\ & + \sum_{p\epsilon P}\sum_{m\epsilon M}\sum_{k\epsilon K} xp_{pkdm}^{(6)t}, \qquad \forall d,t\geq 1\end{aligned} \tag{16}$$

$$EmgIn_{pj}^{\prime t} = EmgIn_{pj}^{\prime t-1} + \sum_{m\epsilon M}\sum_{j\epsilon J} xp_{pijm}^{t} - \sum_{m\epsilon M}\sum_{k\epsilon K} xp_{pjkm}^{\prime\prime t}, \qquad \forall j,p,t\geq 1 \tag{17}$$

$$EmgIn_{pk}^{\prime\prime t} = EmgIn_{pk}^{\prime\prime t-1} + \sum_{m\epsilon M}\sum_{i\epsilon I} xp_{pikm}^{\prime t} + \sum_{m\epsilon M}\sum_{j\epsilon J} xp_{pjkm}^{\prime\prime t} - \sum_{m\epsilon M}\sum_{h\epsilon H} xp_{pkhm}^{\prime\prime\prime t}, \qquad \forall k,p,t\geq 1. \tag{18}$$

– **Strategic stock constraint**

Constraint (19) indicates the total amount of pre-position inventory in main and local DCs over each time period, and the product must be more than strategic stock.

$$\sum_{j\epsilon J} EmgIn'^{t}_{pj} + \sum_{k\epsilon K} EmgIn''^{t}_{pk} \geq \mathrm{SS}^{t}_{p}, \quad \forall p, t. \tag{19}$$

– **Capacity constraints**

The storage capacity limitation in MCs, DCs and DSCs are shown in constraints (20)–(23), respectively.

$$\sum_{p\epsilon P} In^{t-1}_{pi} + \sum_{p\epsilon P}\sum_{l\epsilon L} qnt^{t}_{pil} \leq cap_i y_i, \qquad \forall i, t \geq 1 \tag{20}$$

$$\sum_{p\epsilon P} In'^{t-1}_{pj} + \sum_{p\epsilon P}\sum_{m\epsilon M}\sum_{i\epsilon I} xp^{t}_{pijm} \leq cap'_j w_j, \qquad \forall j, t \tag{21}$$

$$\sum_{p\epsilon P} In''^{t-1}_{pk} + \sum_{p\epsilon P}\sum_{m\epsilon M}\sum_{i\epsilon I} xp'^{t}_{pikm} + \sum_{p\epsilon P}\sum_{m\epsilon M}\sum_{j\epsilon J} xp''^{t}_{pjkm} \leq cap''_k z_k, \qquad \forall k, t \tag{22}$$

$$\sum_{p\epsilon P}\sum_{m\epsilon M}\sum_{i\epsilon I} xp^{(4)t}_{pidm} + \sum_{p\epsilon P}\sum_{m\epsilon M}\sum_{j\epsilon J} xp^{(5)t}_{pjdm} + \sum_{p\epsilon P}\sum_{m\epsilon M}\sum_{k\epsilon K} xp^{(6)t}_{pkdm} \leq cap'''_d u_d, \qquad \forall d, t. \tag{23}$$

– **Perished product flows balance constraint**

Constraints (24)–(26) dedicate the perished pharmaceutical product flows. So, the products flow from MCs, main and local DCs to DSCs over each time period must be equal to the number of perished products in the same centers.

$$\sum_{m\epsilon M}\sum_{d\epsilon D} xp^{(4)t}_{pidm} = \lambda^{t}_{p} In^{t-1}_{pi}, \qquad \forall p, i, t \geq 1 \tag{24}$$

$$\sum_{m\epsilon M}\sum_{d\epsilon D} xp^{(5)t}_{pjdm} = \lambda'^{t}_{p} In^{t-1}_{pj}, \qquad \forall p, j, t \geq 1 \tag{25}$$

$$\sum_{m\epsilon M}\sum_{d\epsilon D} xp^{(6)t}_{pkdm} = \lambda''^{t}_{p} In^{t-1}_{pj}, \qquad \forall p, k, t \geq 1. \tag{26}$$

– **Node criticality constraints**

Equations (27)–(30) are node criticality constraints for MCs, main and local DCs, and DSCs, respectively, which are already described in Section 3.2.2.

$$\left(U^{t}_{i} - \left(\sum_{p\epsilon P}\sum_{l\epsilon L} qnt^{t}_{pil} + \sum_{j\epsilon J}\sum_{p\epsilon P}\sum_{m\epsilon M} xp^{t}_{pijm} + \sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{k\epsilon K} xp'^{t}_{pikm}\right)\right)(1 - y'_i) \geq \varepsilon(1 - y'_i), \qquad \forall i, t \tag{27}$$

$$\left(U'^{t}_{j} - \left(\sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{i\epsilon I} xp^{t}_{pijm} + \sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{k\epsilon K} xp''^{t}_{pjkm}\right)\right)\big(1 - w'_j\big) \geq \varepsilon\big(1 - w'_j\big), \qquad \forall j, t \tag{28}$$

$$\begin{aligned}&\left(U''^{t}_{k} - \left(\sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{i\epsilon I} xp'^{t}_{pikm} + \sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{j\epsilon J} xp''^{t}_{pjkm} + \sum_{m\epsilon M}\sum_{p\epsilon P}\sum_{h\epsilon H} xp'''^{t}_{pkhm}\right)\right)(1 - z'_k)\\ &\qquad \geq \varepsilon(1 - z'_k), \qquad \forall k, t\end{aligned} \tag{29}$$

$$\begin{aligned}&\left(U^{(4)t}_{d} - \left(\sum_{k\epsilon K}\sum_{w\epsilon W}\sum_{i\epsilon N} xp^{(4)t}_{idm} + \sum_{k\epsilon K}\sum_{w\epsilon W}\sum_{i\epsilon N} xp^{(5)t}_{jdm} + \sum_{k\epsilon K}\sum_{w\epsilon W}\sum_{i\epsilon N} xp^{(6)t}_{kdm}\right)\right)(1 - u'_d)\\ &\qquad \geq \varepsilon(1 - u'_d), \qquad \forall d, t.\end{aligned} \tag{30}$$

– **Assignment constraints (Flow complexity constraints)**

Constraints (31)–(37) are assignment constraints and make the interaction between the nodes if a product flow exists. These constraints, also known as flow complexity constraints, facilitate counting the number of links between nodes for the resilience objective function (Z_4).

$$\sum_{p \epsilon P} \sum_{m \epsilon M} xp^{t}_{pijm} \leq M\nu^{t}_{ij}, \qquad \forall i, j, t \tag{31}$$

$$\sum_{p \epsilon P} \sum_{m \epsilon M} xp'^{t}_{pikm} \leq M\nu'^{t}_{ik}, \qquad \forall i, k, t \tag{32}$$

$$\sum_{p \epsilon P} \sum_{m \epsilon M} xp''^{t}_{pjkm} \leq M\nu''^{t}_{jk}, \qquad \forall j, k, t \tag{33}$$

$$\sum_{p \epsilon P} \sum_{m \epsilon M} xp'''^{t}_{pkhm} \leq M\nu'''^{t}_{kh}, \qquad \forall k, h, t \tag{34}$$

$$\sum_{p \epsilon P} \sum_{m \epsilon M} xp^{(4)t}_{pidm} \leq M\nu^{(4)t}_{id}, \qquad \forall i, d, t \tag{35}$$

$$\sum_{p \epsilon P} \sum_{m \epsilon M} xp^{(5)t}_{pjdm} \leq M\nu^{(5)t}_{jd}, \qquad \forall j, d, t \tag{36}$$

$$\sum_{p \epsilon P} \sum_{m \epsilon M} xp^{(6)t}_{pkdm} \leq M\nu^{(6)t}_{kd}, \qquad \forall k, d, t. \tag{37}$$

– **Lower and upper bound for disposal operation**

In DSCs, there are lower and upper bound for disposal operations shown in constraints (38) and (39), respectively.

$$\sum_{t \epsilon T} \sum_{p \epsilon P} qnt'^{t}_{dp} \geq \delta_d, \qquad \forall d \tag{38}$$

$$\sum_{t \epsilon T} \sum_{p \epsilon P} qnt'^{t}_{dp} \leq \Delta_d, \qquad \forall d. \tag{39}$$

– **Transitional probability calculation**

The transitional probability of production is calculated by equations (40) and (41). For more clarity, these constraints calculate the probability of each transitioned product to a specific allocated production level in MCs over each technology and time period in order to be employed in production capacity constraint (see Eq. (42)).

$$P^{at}_{pil} = 1 - pd^{t}_{il}, \qquad \forall p, i, l, a = 1, t \tag{40}$$

$$P^{at}_{pil'} = \left(1 - pd^{t}_{il'}\right) \sum_{l}^{l'} \frac{pd^{t}_{il}}{1 - pd^{t}_{il}} P^{a-1,t}_{pil} n^{a-1,t}_{pil}, \qquad \forall p, i, l, a > 1, t. \tag{41}$$

– **Production capacity constraint**

Constraint (42) implies the maximum capacity of each product in MCs at a specific technology.

$$\sum_{a \epsilon A} P^{at}_{pil} qnt^{t}_{pil} \leq \theta_{pil}, \quad \forall p, i, l, t. \tag{42}$$

– **The non-failable technology constraint**

The multiple assignments, one of the resilience measures, is ensured by constraint (43) that the non-failable technology would eventually be assigned to the production if all previous technologies had been disrupted.

$$\sum_{l \neq l+1} n_{pil}^{at} + \sum_{a'}^{a} n_{pil+1}^{a't} = 1, \quad \forall p, i, a, t. \tag{43}$$

– **Other production constraints**

Constraint (44) guarantees that each technology must be assigned to a production level. Constraint (45) is an assignment constraint that joins the variable of production quantity (qnt_{pil}^{t}) to its binary variable (n_{pil}^{at}). Constraints (46) and (47) ensure that the production and disposal operation occur if the corresponding MC and DSC are established.

$$\sum_{a \epsilon A} n_{pil}^{at} = 1, \qquad \forall p, i, l, t \tag{44}$$

$$qnt_{pil}^{t} \leq M \sum_{a \epsilon A} n_{pil}^{at}, \qquad \forall p, i, l, t \tag{45}$$

$$n_{pil}^{at} \leq y_i, \qquad \forall p, i, l, t \tag{46}$$

$$qnt_{dp}^{\prime t} \leq M u_d, \qquad \forall d, p, t. \tag{47}$$

– **Selling and buying of technologies constraints**

Constraints (48) and (49) assure that selling and buying the new technologies will be non-allowable if they take place in the previous or next time period. Constraint (50) guarantees that technologies can be sold if they are bought during the last time period. Similarly, constraint (51) ensures that the technology cannot be sold again after buying. Constraints (52)–(54) are also assignment constraints that make a linkage between the production variables and the selling and buying of technology variables. Constraint (55) assures that the technologies can only be sold if the corresponding MC has already been established.

$$tp_{in}^{t} \leq 1 - tp_{in}^{t'}, \qquad \forall i, n, t, t' \leq t \tag{48}$$

$$tncc_{il}^{t} \leq 1 - tncc_{il}^{t'}, \qquad \forall i, l, t, t' \leq t \tag{49}$$

$$\sum_{t'=t}^{T} tncc_{in}^{t'} \leq \sum_{t'=1}^{t} tp_{in}^{t'}, \qquad \forall i, n \tag{50}$$

$$tp_{in}^{t} \leq 1 - tncc_{in}^{t'}, \qquad \forall i, n, t, t' \leq t \tag{51}$$

$$n_{inp}^{at} \leq \sum_{t'=1}^{t} tp_{in}^{t'}, \qquad \forall i, n, a, t \tag{52}$$

$$n_{pil}^{at} \leq 1 - tncc_{il}^{t'}, \qquad \forall i, l, a, t, t' \leq t \tag{53}$$

$$tp_{in}^{t} \leq \sum_{t'=t}^{T} \sum_{a \in A} n_{inp}^{at}, \qquad \forall i, n, t \tag{54}$$

$$tncc_{il}^{t} \leq y_i, \qquad \forall i, l, t. \tag{55}$$

– **Carbon credit constraints**

Constraints (56) and (57) imply the maximum CO_2 emissions allowed for MCs and DSCs over each time period. Constraints (58) and (59) guarantee that the number of carbon units does not exceed the maximum allowable carbon credit to sell and buy over each time period. Constraint (60) enforces that the variables of selling and buying carbon credits cannot take a value simultaneously.

$$\sum_{n\epsilon N}\left[y_i set^t_{in} + \sum_{p\in P} pef'^t_{pin}(qnt^t_{pin})qnt^t_{pin} - ae^t_i y_i\right] + \sum_{o\epsilon O}\left[y_i set^t_{io} + \sum_{p\in P} pef'^t_{pio}(qnt^t_{pio})qnt^t_{pio} - ae^t_i y_i\right] + ncc^{-t}_i - ncc^{+t}_i \leq 0, \qquad \forall i,t \tag{56}$$

$$\sum_{p\epsilon P} de''^t_{pd}(qnt'^t_{pd})qnt'^t_{pd} \leq ae'^t_d u_d, \qquad \forall d,t \tag{57}$$

$$ncc^{-t}_i \leq ncc^{-\max}_i, \qquad \forall i,t \tag{58}$$

$$ncc^{+t}_i \leq ncc^{+\max}_i, \qquad \forall i,t \tag{59}$$

$$ncc^{-t}_i ncc^{+t}_i = 0, \qquad \forall i,t. \tag{60}$$

Finally, constraints (61) and (62) define the positive and binary variables.

$$In^t_{pi}, In'^t_{pj}, In''^t_{pk}, In'''^t_{dp}, EmgIn'^t_{pj}, EmgIn''^t_{pk}, qnt^{t}_{pil}, qnt'^t_{dp}, xp^t_{pijm}, xp'^t_{pikm}, xp''^t_{pjkm}, xp'''^t_{pkhm}, xp^{(4)t}_{pidm}, xp^{(5)t}_{pjdm}, xp^{(6)t}_{pkdm}, ncc^{-t}_i, ncc^{+t}_i, \Phi \geq 0, \qquad \forall i,j,k,d,h,l,p,m,t \tag{61}$$

$$y_i, w_j, z_k, u_d, y'_i, w'_j, z'_k, u'_d, \nu^t_{ij}, \nu'^t_{ik}, \nu''^t_{jk}, \nu'''^t_{kh}, \nu^{(4)t}_{id}, \nu^{(5)t}_{jd}, \nu^{(6)t}_{kd}, n^{at}_{pil}, tp^t_{il}, tncc^t_{il} \in \{0,1\}, \qquad \forall i,j,k,d,h,l,t. \tag{62}$$

4. Solution approach

The present model is multi-objective mathematical programming that requires to be solved through an efficient approach. In this section, Lexicographic Goal Programming (LGP) is proposed to solve the multi-objective model. An evolutionary algorithm has also been described in the rest of this section to be implemented in the model with large-scale input parameters. As demonstrated in Figure 2 a flowchart showing how the model is implemented and the algorithms work.

4.1. Lexicographic goal programming

In multi-objective optimization models, there is no solution to optimize all the objectives simultaneously. On the other hand, numerous approaches have been developed to solve multi-objective mathematical models. Meanwhile, Charnes and Cooper [45] proposed the goal programming approach to deal with multi-objective models. The main idea of this approach is to bring the optimal solutions nearer to the ideal point, considering the weighting coefficients of objectives. Thus, decision-makers should determine each objective function's goals, and their deviations from goals are minimized, called aspiration levels. Furthermore, the lexicographic achievement procedure is applied to the goal programming model in which an ordered priority levels vector links the deviation variables to the corresponding priority level [46]. In other words, this procedure attempts to optimize the lowerpriority objectives after higherpriority ones have been optimized. Tzeng and Huang [47] have described the general structure of lexicographic goal programming as follows:

$$\min \sum_{j=1}^{J} p_j \left[\sum_{i=1}^{n}\left(\frac{w^-_i d^-_i + w^+_i d^+_i}{k_i}\right)^{\rho}\right]^{1/\rho}, \qquad \rho \geq 1 \tag{63}$$

s.t.

$$g(x) \leq 0, \qquad (\text{or } Ax \leq b) \tag{64}$$

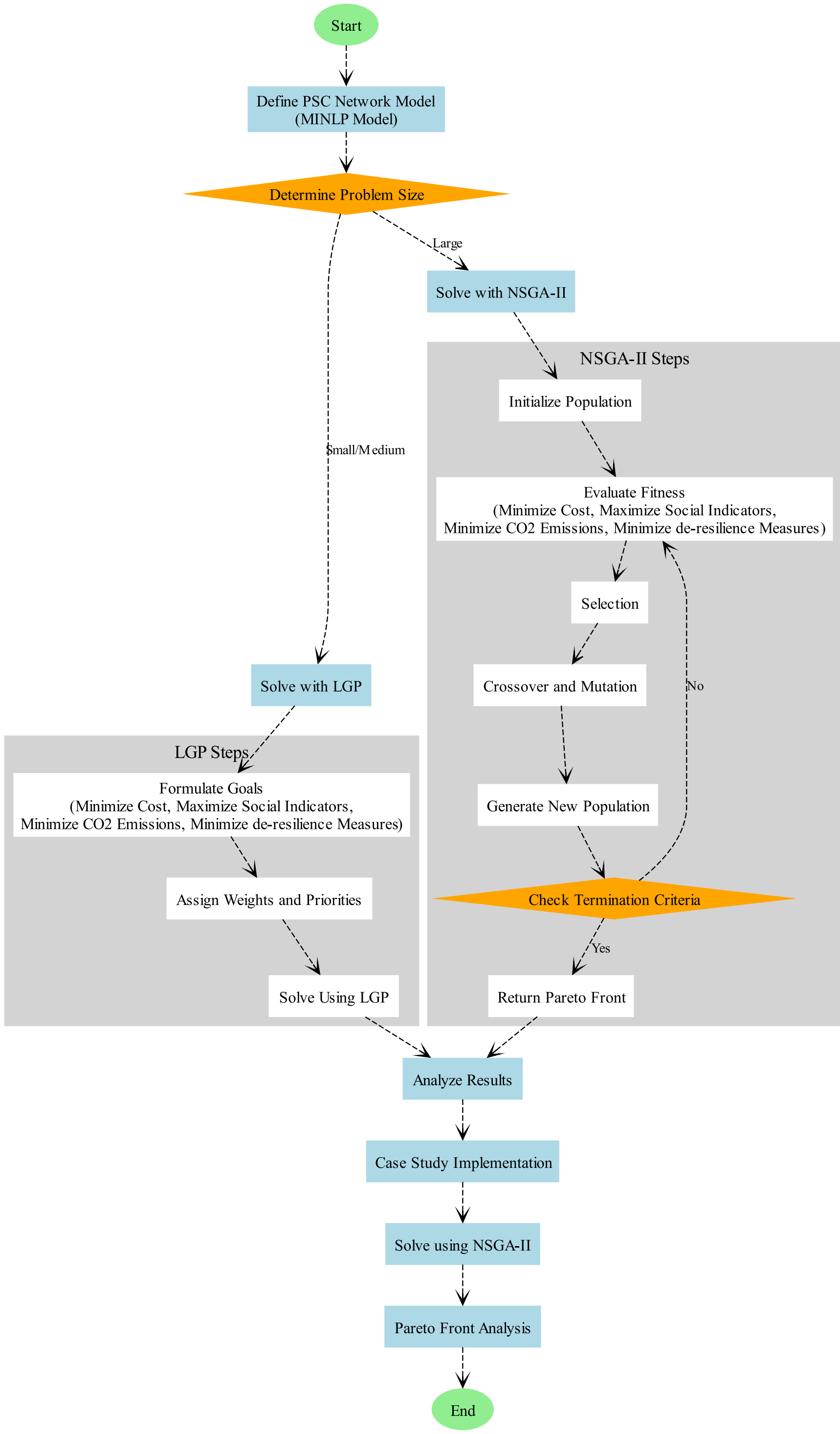


FIGURE 2. Flowchart of the model and algorithms implementation.

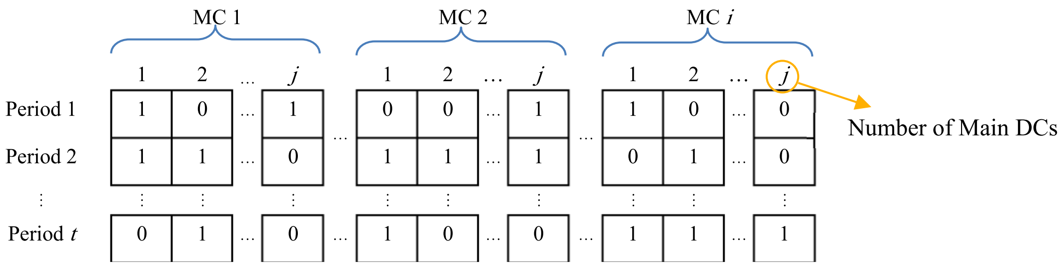


FIGURE 3. An example of chromosome structure representation.

$$f_i(x) + d_i^- - d_i^+ = t_i, \qquad i = 1, \ldots, n, \tag{65}$$
$$d_i^-, d_i^+ \geq 0, \tag{66}$$
$$p_1 \succ p_2 \succ \ldots \succ p_l, \qquad l \leq n \tag{67}$$

where d_i^- and d_i^+ define the negative and positive deviations of objective functions, respectively. Besides, w_i^- and w_i^+ are weighting coefficients. The model is normalized by k_i ($k_i = t_i/100$) and t_i denotes the goal value set by decision-makers. L_p-norm is utilized to find the solution and determine the distance between the goals and the objective functions. Equation (63) shows the objective function of the lexicographic goal programming model. Moreover, equation (64) illustrates the constraints of the proposed model, and equation (66) is the non-negativity constraint for deviation variables. Finally, equation (67) implies the priority operation, if $p_i \succ p_j$, the jth objective must be optimized after the ith objective.

4.2. Evolutionary algorithm

Due to the NP-hard nature of large-scale optimization problems, different methods have been developed, such as Benders decomposition, Lagrangian relaxation, (meta) heuristic method, and evolutionary algorithm [16, 48–50]. Meanwhile, NSGA-II is one of the most efficient and popular evolutionary algorithms used to solve multi-objective problems, developed by Deb *et al.* [51]. In this study, NSGA-II is employed to solve the proposed PSC network problem efficiently with large-scale input data and further achieve the Pareto optimal solution.

The chromosome structure in NSGA-II is crucial, encapsulating information about the supply chain configuration, including MCs, main and local DCs, demand points, and DSCs. Each chromosome is represented as a concatenated array of genes, each corresponding to a specific decision variable or set of related decision variables. For example, a chromosome can be structured with segments indicating the allocation of products from MCs to main DCs. A gene array for the aforementioned chromosome is illustrated in Figure 3.

Some assumptions and NSGA-II parameters are as follows:

- The initial population is generated with uniform distribution randomly.
- An arithmetic crossover operator is used [52] to create new offspring.
- The Gaussian mutation operator is performed [53], whereby a random value is specified to each individual using Gaussian distribution.
- The crowding distance for a set of individuals can be calculated as follows:

$$d_i = \sum_{j=1}^{k} \left| \frac{f_j^{i+1} - f_j^{i-1}}{f_j^{\max} - f_j^{\min}} \right| \tag{68}$$

where d_i is the crowding distance of the ith individual, and k is the number of objective functions. Also, f_j^{i+1} and f_j^{i-1} dedicate the jth objective function of the $(i-1)$th and $(i+1)$th individual, and $f_j^{\max}$ and $f_j^{\min}$ and minimum value of the jth objective function, respectively.

– The crossover and mutation percentages are set to 0.7 and 0.3, respectively.
– The number of the initial population (n-Pop) is set to 300.
– The maximum number of function calls (NFCs) is set to 1200.
– The number of maximum runs for algorithms is set to 10.

5. Numerical results

The NSGA-II was coded in MATLAB R2021a for largescale problems, and BARON 18.5.8 solver in GAMS 25.1.2 was used to solve the problems from small to medium scale in a Laptop with Intel Core i7 CPU, 2.20 GHz and 8 GB of RAM. In the following, the validation of the proposed model is explained, and then the case study and sensitivity analysis are described, as well as the results.

5.1. Validation

In order to validate the proposed evolutionary algorithm for the largescale PSC problem, twenty test problems of different sizes have been solved by the BARON solver in GAMS. Table 3 demonstrates the specification of these twenty test problems as well as the number of equations, total variables and binary variables for each problem. Five components specify each problem: the number of MCs, main and local DCs, DSCs and demand points, respectively. The input parameters for test problems are generated randomly by the uniform distribution provided in Table A.1 in appendix. Additionally, the prespecified thresholds of node criticality (*i.e.*, U_i^t, $U_j^{\prime t}$, $U_k^{\prime\prime t}$ and $U_d^{\prime\prime\prime t}$) and aspiration levels are recalculated for each specified test problem. Also, weighting coefficients and preempt levels for objective functions are considered similarly in the lexicographic goal programming problem. According to the results (see Tab. 4), when the size of the problem increases, the CPU time also increases significantly to the point that the maximum allotted time for a solution (8 h) has been exceeded in problem No. 15. In other words, the exact method couldn't solve problems larger than $12 \times 13 \times 15 \times 5 \times 16$, while the case study has a $31 \times 31 \times 31 \times 31 \times 31$ size problem. According to the complex modeling relationships and a multitude of binary variables, the necessity of implementing an efficient evolutionary algorithm such as NSGA-II becomes more apparent than before.

Additionally, different types of resilience considerations in the proposed PSC model are compared in Table 5 based on a resilience indicator. As the results show, the model without resilience strategies has the highest value. Compared to the non-resilient model, subsequent models have improvements, but the resilient model with strategies category (III) (*i.e.*, inventory management strategies) has been considerable. Notably, although the resilient model with strategies categories (I) and (II) have not been improved much individually, the fully resilient model with integrated strategies has significant improvement. Figure 4 illustrates a comparison between the improvement levels of resilient model types. Consequently, the superiority of the fully resilient model over the other ones is aimed at its network resilience level.

5.2. Case study

Iran was the second country that had announced two coronavirus deaths within 50 days after China. After 2 years, Iran is still one of the countries with the newest COVID-19 cases and deaths. Although this situation requires efficient strategies to be manipulated, they may effectively deal with the outbreak or cause issues. An efficient strategy to reduce the mortality rate is to deliver the medicines adequately and timely by designing a PSC network. Manufacturers play a significant role in the PSC network in Iran since they supply more than 95% of the medicines market in terms of volume [54]. Thus, any disruption in the manufacturing centers would have a severe impact on PSC and consequently could affect people's healthcare.

In this regard, with efficient resilience strategies and solution methods, the proposed PSC model can be usefully implemented in a case study of Iran. Figure 5 represents the 31 major cities in Iran (the capital of Iran's provinces) as demand points in which MCs, main and local DCs and DSCs can be established. The planning horizon in this study is set to be $T = 8$ with a season (four months) per unit. Also, the three main

TABLE 3. Some characteristics of the test problems.

Problem no.	Problem specifications ($i \times j \times k \times d \times h$)	No. of equations	No. of total variables	No. of binary variable
1	$1 \times 1 \times 2 \times 1 \times 2$	889	613	217
2	$1 \times 1 \times 2 \times 1 \times 3$	904	637	223
3	$1 \times 1 \times 3 \times 1 \times 4$	973	765	252
4	$1 \times 2 \times 4 \times 2 \times 5$	1143	1113	330
5	$2 \times 3 \times 5 \times 2 \times 6$	2007	1914	603
6	$3 \times 4 \times 6 \times 2 \times 7$	2895	2811	900
7	$4 \times 5 \times 7 \times 2 \times 8$	3807	3804	1221
8	$5 \times 6 \times 8 \times 3 \times 9$	4823	5141	1625
9	$6 \times 7 \times 9 \times 3 \times 10$	5792	6362	2003
10	$7 \times 8 \times 10 \times 3 \times 11$	6785	7679	2405
11	$8 \times 9 \times 11 \times 4 \times 12$	7909	9448	2917
12	$9 \times 10 \times 12 \times 4 \times 13$	8959	10 993	3376
13	$10 \times 11 \times 13 \times 4 \times 14$	10 033	12 634	3859
14	$11 \times 12 \times 14 \times 5 \times 15$	11 265	14 835	4479
15	$12 \times 13 \times 15 \times 5 \times 16$	12 396	16 704	5019
16	$13 \times 14 \times 16 \times 5 \times 17$	13 551	18 669	5583
17	$14 \times 15 \times 17 \times 6 \times 18$	14 891	21 302	6311
18	$15 \times 16 \times 18 \times 6 \times 19$	16 103	23 495	6932
19	$16 \times 17 \times 19 \times 6 \times 20$	17 339	25 784	7577
20	$17 \times 18 \times 20 \times 7 \times 21$	18 787	28 849	8413

TABLE 4. Result of test problems using exact method.

Problem no.	CPU time (s)	Relative gap (%)	Optimal objective value			
			Cost	Social	Environmental	Resilien
1	0.08	4.73E−13	158 012.1	203.654	7236.755	173 968.8
2	0.19	1.57E−13	160 597.4	205.165	7784.789	186 237.4
3	0.25	1.72E−12	154 590.7	249.076	6439.841	100 344.7
4	0.42	1.00E−04	156 703.9	295.830	6632.650	184 416.5
5	0.86	1.00E−04	162 230.8	424.495	7709.554	84 305.09
6	2.37	1.00E−04	158 485.8	746.400	7165.804	165 168.8
7	3.5	1.00E−04	156 243.2	695.005	6704.636	131 782.5
8	6.17	1.00E−04	160 050.9	1073.105	7193.225	188 389.0
9	8.52	1.00E−04	157 896.2	1228.705	6518.229	173 314.0
10	86.05	9.44E−06	159 196.5	1212.292	7827.231	178 294.3
11	2954.34	9.50E−06	157 672.8	1610.910	7960.647	162 856.5
12	280.35	1.00E−04	172 243.5	1685.606	7778.757	186 124.5
13	27 327.93	9.89E−03	173 940.8	1839.430	8530.315	179 658.9
14	8160.84	2.76E−03	169 108.4	1862.096	8458.882	174 502.1
15	28 509.29	2.71E−03	167 510.2	2333.543	8226.922	196 192.6
16	28 800	–	NA*	NA	NA	NA
17	28 800	–	NA	NA	NA	NA
18	28 800	–	NA	NA	NA	NA
19	28 800	–	NA	NA	NA	NA
20	28 800	–	NA	NA	NA	NA

Notes. *Solution is not achieved in 8 h.

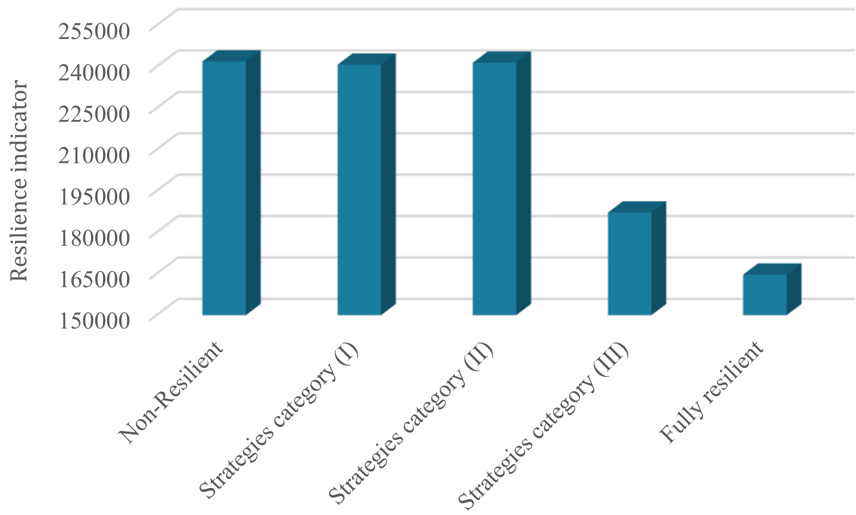
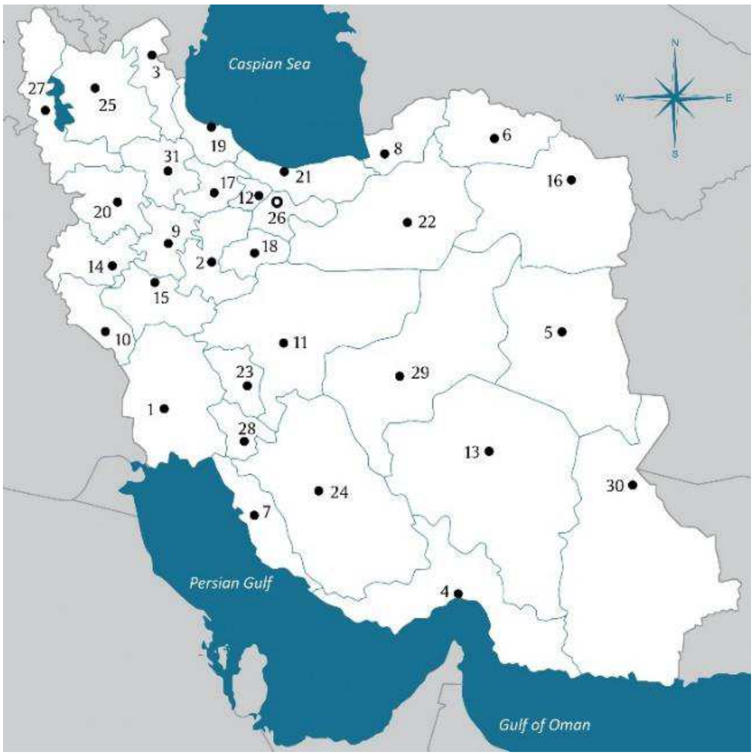


FIGURE 4. Effect of different types of strategies on the improvement of resiliency.



ID	City	ID	City
1	Ahvaz	17	Qazvin
2	Arak	18	Qom
3	Ardabil	19	Rasht
4	Bandar Abbas	20	Sanandaj
5	Birjand	21	Sari
6	Bojnourd	22	Semnan
7	Bushehr	23	Shahrud
8	Gorgan	24	Shiraz
9	Hamadan	25	Tabriz
10	Ilam	26	Tehran
11	Isfahan	27	Urmia
12	Karaj	28	Yasuj
13	Kerman	29	Yazd
14	Kermanshah	30	Zahedan
15	Khorramabad	31	Zanjan
16	Mashhad		

FIGURE 5. Capital of Iran's provinces.

Table 5. Comparison between results of resilient model type.

Row	Resilient model type	Resilience indicator	Improvement (%)
1	Non-resilient mode	241 914.773	0
2	Resilient model: strategies category (I)	240 759.832	0.5
3	Resilient model: strategies category (II)	241 456.051	0.2
4	Resilient model: strategies category (III)	187 196.978	22.6
5	Fully resilient model: integrated strategies	164 703.868	31.9

medicines prescribed for patients are (1) Hydroxychloroquine sulfate, (2) Ritonavir/Lopinavir (for ambulatory patients), and (3) RemdeSivir (for hospitalized patients).

The demand parameter is determined based on the number of patients and the required doses for each patient. According to the "Instructions for Distribution and Use of RemdeSivir" published by the Iran Food and Drug Administration (IFDA), an infected person (adults and children weighting more than 40 kg) requires 200 mg (2 doses) of RemdeSivir on the first day, followed by 100 mg daily for the next four days, resulting in a total of five days of treatment. If no clinical improvement is observed, the treatment can be extended for an additional five days. In total, each infected person needs between 6 and 11 doses.

In Iran, the Ministry of Health and Medical Education (MOH&ME) periodically reports COVID-19 cases and deaths to each province. The time-periodic demand for each drug and city is then calculated by multiplying the number of required doses by the number of patients. The demand parameter, which is based on a lower bound (LB) and upper bound (UB) of demand in each city, is illustrated in Table 6. For instance, the time-periodic demand for Lopinavir/Ritonavir in Mashhad city is represented as $D^t_{16,3} \sim U[1\,175\,202, 1\,880\,323]$.

The establishment cost for each category of facilities, such as MCs, main and local DCs, and DSCs, is divided into two parts. The first part includes the cost of purchasing requirements (*e.g.*, machinery, building materials, office equipment, etc.), which is considered fixed for all cities. In the second part, the cost of buying land is variable, and it is calculated for each city based on the corresponding average transaction value of land (Thousand Rials per m^2). Transportation costs between nodes are obtained by distances between each city provided in Table A.2 in Appendix. The Regional Development Factor is calculated based on three integrated composite indexes for each city by Abdollahzade and Sharifzadeh [55]. Obviously, the higher the value, the more development potential the city has. Thus, Zahedan and Tehran have the highest and lowest potential to be developed, respectively. Also, GDP share is based on each city's share of the total Gross Domestic Product (GDP) in Iran. Table 7 demonstrates the value of these three indicators and the unemployment rate for each city.

5.3. Sensitivity analysis and final results

A set of sensitivity analyses has been conducted on the critical parameters to show the objective function behavior in the real situation of the case study. To this end, the demand parameter (D^t_{ph}) and strategic stock parameter (SS^t_p) are analyzed in an interval of -50% to $+50\%$ by 25% step size. Table 8 indicates the effects of changing these two parameters on objective functions. As the results show, it can clearly be understood that all objective functions will increase by increasing the demand while it was expected, but in contrast, the opposite happens in the case of the strategic stock parameter. Contrary to expectations, an increase in strategic stock leads to a cost reduction, along with an increase and decrease in resilience level and CO_2 emissions, respectively. So, the preparation of an extra strategic stock level can be a good practical insight. Additionally, it should be noted that the social (Z_2) and the resilience (Z_4) objective functions (see Figs. 4b and 5b) are more sensitive than the two other ones. Although all four objective functions have linear behavior with respect to parameter changes, they are more affected by decreasing the parameter rather than its increase (Fig. 6).

Table 6. LB and UB of medicine demand for each city.

City ID	RemdeSivir		Hydroxychloroquine sulfate		Lopinavir/Ritonavir	
	LB	UB	LB	UB	LB	UB
1	374 368	686 342	499 158	623 947	1 247 895	1 996 632
2	126 304	231 557	168 405	210 507	421 013	673 621
3	70 876	129 939	94 501	118 126	236 252	378 003
4	87 231	159 924	116 309	145 386	290 772	465 235
5	84 505	154 927	112 674	140 842	281 685	450 696
6	66 332	121 609	88 443	110 554	221 108	353 772
7	71 784	131 604	95 712	119 640	239 281	382 849
8	159 016	291 529	212 021	265 026	530 052	848 084
9	144 477	264 875	192 636	240 795	481 590	770 545
10	49 976	91 623	66 635	83 294	166 588	266 541
11	365 282	669 683	487 042	608 803	1 217 606	1 948 170
12	143 568	263 209	191 425	239 281	478 562	765 699
13	227 165	416 470	302 887	378 609	757 218	1 211 548
14	165 376	303 190	220 502	275 627	551 255	882 007
15	143 568	263 209	191 425	239 281	478 562	765 699
16	352 561	646 361	470 081	587 601	1 175 202	1 880 323
17	77 236	141 600	102 982	128 727	257 454	411 926
18	139 934	256 545	186 578	233 223	466 446	746 314
19	187 184	343 171	249 579	311 974	623 947	998 316
20	128 121	234 889	170 828	213 535	427 071	683 313
21	296 224	543 077	394 965	493 706	987 412	1 579 859
22	107 222	196 574	142 963	178 703	357 407	571 851
23	65 424	119 943	87 231	109 039	218 079	348 926
24	332 570	609 712	443 427	554 283	1 108 567	1 773 707
25	257 151	471 444	342 868	428 585	857 170	1 371 473
26	838 694	1 537 606	1 118 259	1 397 824	2 795 648	4 473 037
27	260 786	478 107	347 714	434 643	869 286	1 390 858
28	61 789	113 280	82 385	102 982	205 963	329 541
29	184 458	338 173	245 944	307 430	614 861	983 777
30	59 063	108 282	78 751	98 438	196 877	315 003
31	93 592	171 586	124 789	155 987	311 974	499 158

Based on the real-world input data, the proposed PSC network was solved with MATLAB, and 23 Pareto solutions were obtained with a CPU time of 747 s. Figure 7 illustrates the optimum PSC network in Iran. As a result, the total network cost equals 3 423 414.769 billion Rials (equivalent to $11 411 million). With the establishment of these facilities, up to 16 488 job opportunities could be created. The environmental objective function is equal to 539 659.9383, which is an acceptable value for this problem according to the carbon emission trading or cap-and-trade strategy [56]. At first, although it seems that the total network cost is enormous, it's justifiable. As shown in Figure 8, a significant number of MCs are assumed to be established. So, related fixed costs and production costs, which constitute a considerable contribution, lead to an increase in total network costs. More precisely, this number of established manufacturers is due to the high demand for medicine in Iran, which further imposes a high cost that the government or companies may not be able to afford. Therefore, the import policy is a beneficial way to meet the unsatisfied demand.

Additionally, the Pareto front solutions generated by the proposed evolutionary algorithm for all four objectives are detailed in Table 9 and illustrated in Figures 9–13. These results demonstrate the superiority of the NSGA-II algorithm in delivering high-quality non-dominated solutions. By examining these Pareto front solu-

TABLE 7. Extra information to compute case study input parameters.

City ID	Unemployment rate (%)	GDP share (%)	Regional development factor (%)	Land value per m^2	City ID	Unemployment rate (%)	GDP share (%)	Regional development factor (%)	Land value per m^2
1	14.7	5.52	47.3	50 960	17	8.2	1.79	43.5	85 490
2	8.3	2.1	43.1	81 100	18	10.3	1.14	45.7	83 570
3	9	1.15	65	49 640	19	9.6	2.63	63.3	45 130
4	14.1	2.13	59.2	44 890	20	12.2	1.05	65.7	47 020
5	8.7	0.59	67.7	36 100	21	8.9	3.9	56.4	47 900
6	7.6	0.62	60.8	38 960	22	7.9	1.04	38.6	66 120
7	10.4	6.26	46	38 750	23	13.9	0.76	58.1	60 670
8	11.1	1.38	62.1	33 710	24	7.6	5.32	60	80 570
9	5.3	1.49	57.4	44 160	25	9.1	4.04	53.7	76 850
10	8.7	0.62	57.6	46 650	26	10.7	25.9	33.1	705 470
11	10.3	6.67	40.9	114 790	27	8.6	2.33	61.2	49 260
12	13	3.3	48.9	78 030	28	9.9	0.69	72.4	10 390
13	10.7	3.64	58	41 110	29	15.1	2.15	46.1	37 630
14	14	1.73	68.6	38 260	30	15.2	1.63	89.2	47 510
15	14.7	1.32	75.2	28 320	31	5.1	1.2	53.9	56 990
16	8.9	5.83	54.6	45 040					

TABLE 8. Change in parameters *vs.* change in objective functions.

Parameter	Change in parameter	Change in objective function (%)			
		Z_1	Z_2	Z_3	Z_4
D_{ph}^t	−50%	−12.0	−48.6	−37.6	−44.2
	−25%	−6.7	−24.1	−18.7	−22.6
	0	0.0	0.0	0.0	0.0
	+25%	5.8	24.4	19.7	21.7
	+50%	11.9	48.5	38.0	43.5
SS_p^t	−50%	25.3	98.2	77.1	89.5
	−25%	7.3	33.0	26.0	30.0
	0	0.0	0.0	0.0	0.0
	+25%	−5.1	−19.6	−15.4	−18.1
	+50%	−8.1	−32.6	−25.1	−30.3

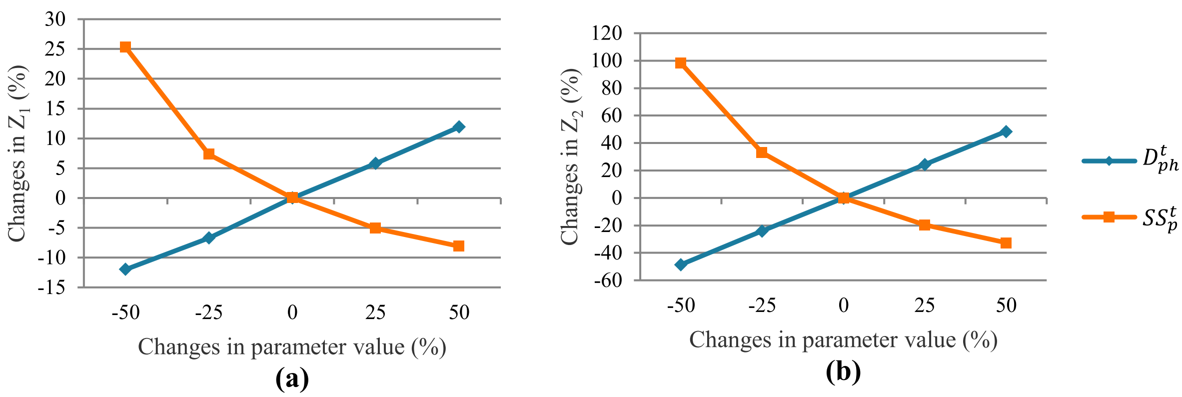


FIGURE 6. The results of sensitivity analysis for Demand and Strategic stock parameters on Z_1 and Z_2.

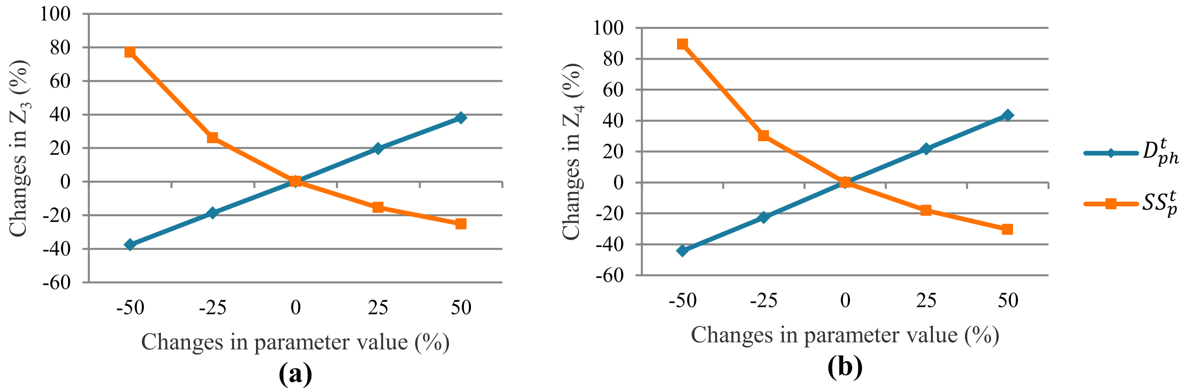


FIGURE 7. The results of sensitivity analysis for Demand and Strategic stock parameters on Z_3 and Z_4.

tions, decision-makers can better understand the trade-offs involved in satisfying conflicting objectives and make more informed choices that align with their strategic priorities.

Table 9 presents the Pareto front solutions for the Iran case study problem, highlighting the trade-offs between the cost objective (Z_1), social objective (Z_2), environmental objective (Z_3), and resilience objective (Z_4). The table includes 23 Pareto solutions, each representing a different balance between these objectives. The Pareto front diagrams in Figures 7–9 illustrate the trade-off relationships between pairs of objective functions. Notably, the best value for the social objective (Z_2), which is a maximization objective, appears as the lowest value in the table because it is multiplied by a negative sign for calculation purposes. For example, as the cost objective function (Z_1) increases, the social objective (Z_2) initially decreases steeply, then continues to decrease almost linearly, and finally stabilizes with minimal further change.

To provide a more comprehensive view, the Pareto front solutions are also plotted in a three-dimensional space in Figures 12 and 13. These figures depict the trade-off relationships between three objective functions simultaneously, offering a clearer visualization of the complex interactions and compromises required to balance multiple objectives.

From the Pareto front solutions, several key insights can be drawn. There is a clear trade-off between the cost objective (Z_1) and the social objective (Z_1). As the cost increases, the social objective tends to decrease. The environmental objective (Z_3) shows variability across the solutions, with higher environmental values generally associated with lower costs. For example, Solution 4 has a high environmental value (563 731.8094) and a lower cost, indicating that cost-effective solutions can also be environmentally beneficial. The resilience objective (Z_4) tends to increase with better social and environmental outcomes. For instance, Solution 4, which has a high resilience value (410 346.0787), also has favorable social and environmental values, suggesting that resilience can be improved alongside other objectives. Some solutions offer a balanced trade-off between all objectives. For example, Solution 16 has moderate values across all objectives, indicating a well-rounded approach that does not overly sacrifice any single objective.

5.4. Managerial insights

Concise insights from the study provide a novel perspective for decision-makers on pharmaceutical supply chain networks. The sensitivity analyses and case study information offer valuable managerial insights and suggestions. Here are some key takeaways:

– The integration of resilience strategies has proven effective in enhancing the supply chain's flexibility and robustness against disruptions. These strategies, while potentially incurring additional costs, significantly improve the network's resilience, which is a crucial macro-level goal.

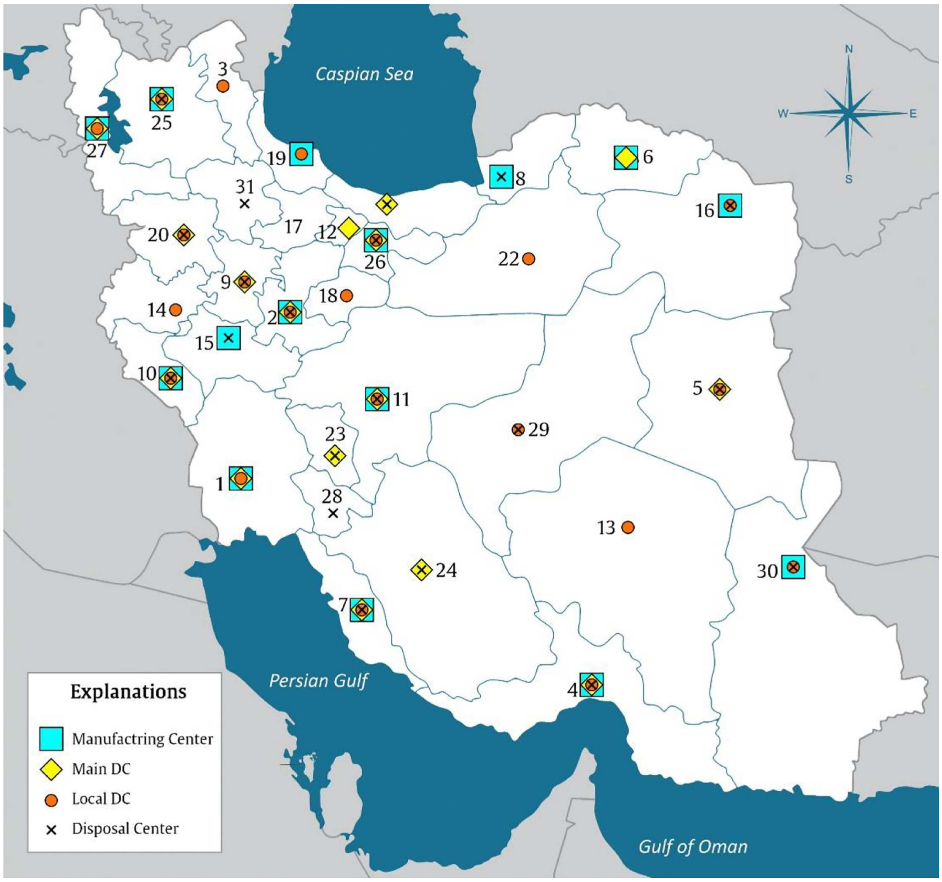


FIGURE 8. Optimum PSC network in Iran.

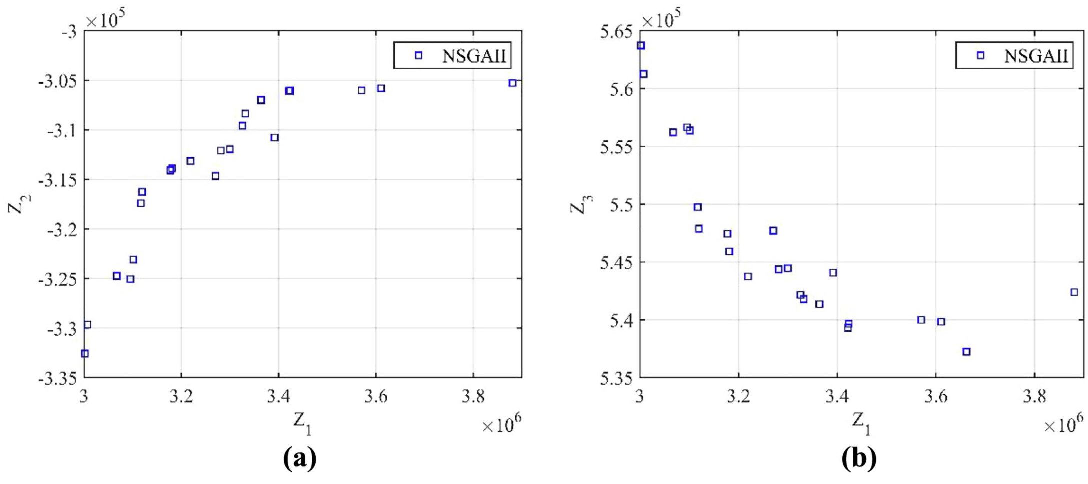


FIGURE 9. Pareto front solutions in two-dimensional space: (a) cost-social, (b) cost-environmental.

TABLE 9. Pareto front solutions for the Iran case study problem.

No. of pareto solution	Pareto front solution			
	Z_1 (Cost)	Z_2 (Social)	Z_3 (Environ∼)	Z_4 (Resilience)
1	3 423 414.769	−306 064.1253	539 659.9383	386 576.3821
2	3 880 554.479	−305 282.334	542 403.7713	387 515.3145
3	3 662 072.252	−303 009.5606	537 239.6815	388 389.5206
4	3 001 839.066	−332 573.4079	563 731.8094	410 346.0787
5	3 117 015.908	−317 402.2534	549 743.6891	396 533.1771
6	3 007 070.147	−329 645.6853	561 254.1807	408 771.5093
7	3 095 364.455	−325 053.0705	556 650.5338	403 299.7332
8	3 067 252.476	−324 733.9541	556 219.007	404 109.0188
9	3 119 246.027	−316 262.8643	547 893.5217	396 059.6359
10	3 101 019.533	−323 087.7156	556 371.665	403 373.0505
11	3 570 174.111	−306 025.3972	539 993.9726	389 359.9589
12	3 177 231.702	−314 081.4698	547 451.4176	393 516.1624
13	3 363 871.979	−306 991.5645	541 346.1668	389 718.3366
14	3 218 863.512	−313 129.5124	543 749.2846	393 005.6208
15	3 331 465.895	−308 361.2692	541 786.3268	390 927.6229
16	3 180 911.574	−313 875.0329	545 911.6299	393 153.8915
17	3 391 486.629	−310 758.1241	544 079.6248	389 313.2386
18	3 270 363.656	−314 661.171	547 714.2346	392 256.4423
19	3 610 598.743	−305 805.6377	539 830.568	388 116.7495
20	3 421 367.988	−306 064.8637	539 312.4375	388 259.2239
21	3 299 663.747	−311 958.4014	544 453.7099	392 788.3276
22	3 325 365.462	−309 585.4971	542 170.8496	392 654.2306
23	3 281 143.227	−312 082.6476	544 366.4254	391 510.649

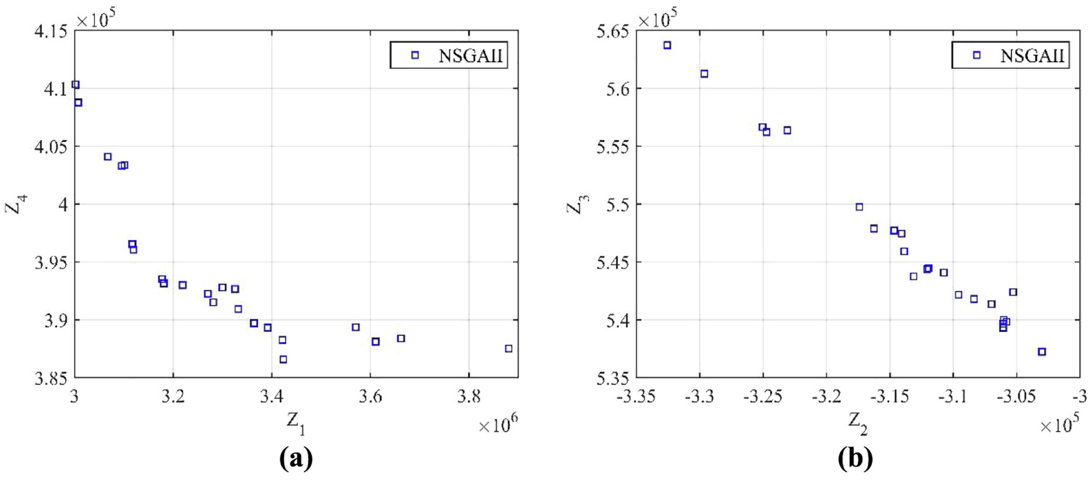


FIGURE 10. Pareto front solutions in two-dimensional space: (a) cost-resilience, (b) social-environmental.

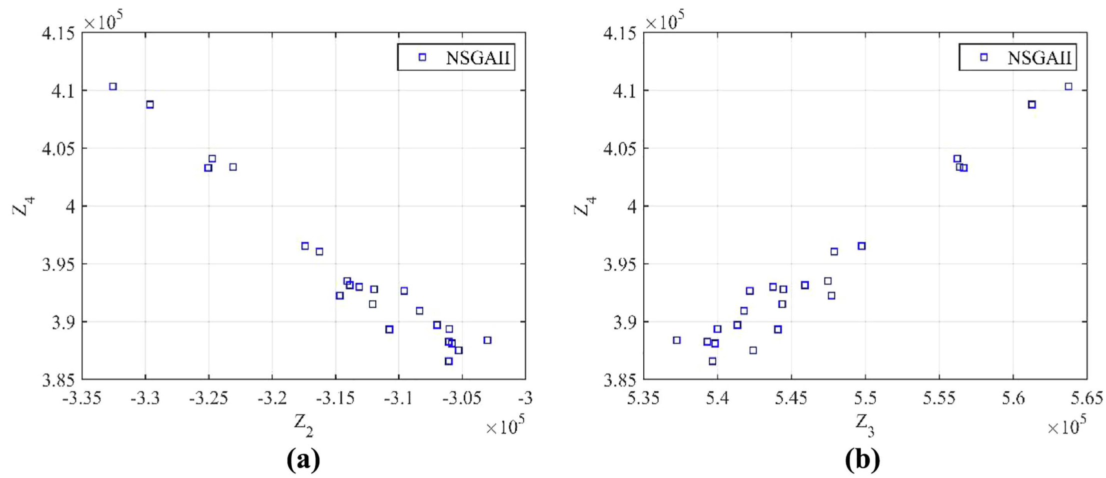


FIGURE 11. Pareto front solutions in two-dimensional space: (a) social-resilience, (b) environmental-resilience.

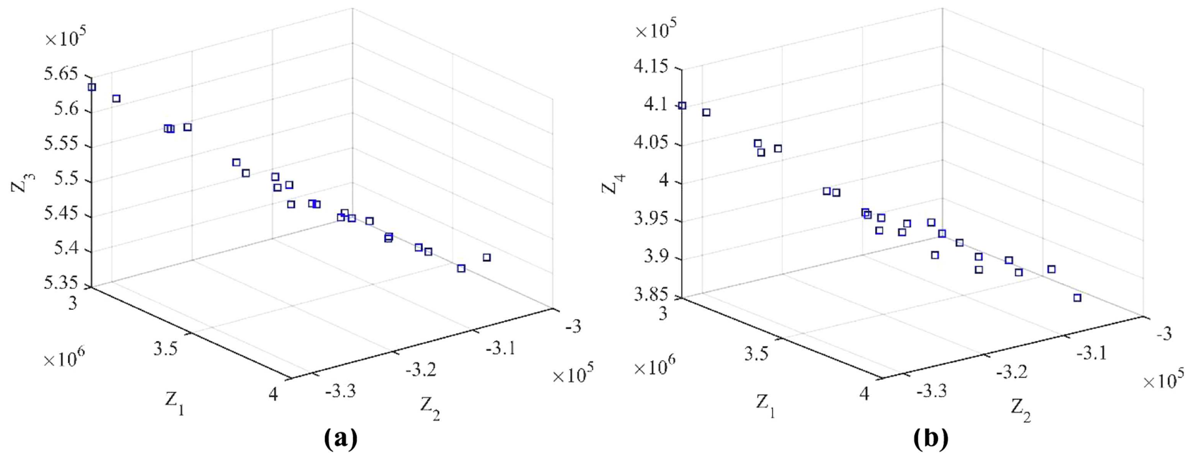


FIGURE 12. Pareto front solution in three-dimensional space: (a) social-cost-environmental, (b) social-cost-resilience.

- An increase in production costs, particularly more than 20%, leads to a sharp decline in manufacturers' operational efficiency. This highlights the importance of efficient cost management and the need for continuous improvement in production processes to maintain overall supply chain performance.
- Managers should minimize CO_2 emissions across the supply chain by using eco-friendly technologies and optimizing transportation routes. Establishing facilities in high-unemployment, low-GDP regions can enhance social sustainability by creating jobs and fostering regional development.
- Investing in non-failable and advanced technologies can reduce production disruptions and enhance supply chain efficiency. Regularly upgrading old technologies and reallocating resources helps maintain production levels and mitigate disruption impacts.
- Conducting sensitivity analyses to validate the supply chain model provides insights into the behavior of different objective functions under various scenarios. This helps in making informed decisions and preparing for potential risks. For example, The sensitivity analysis showed that resilience measures significantly impact

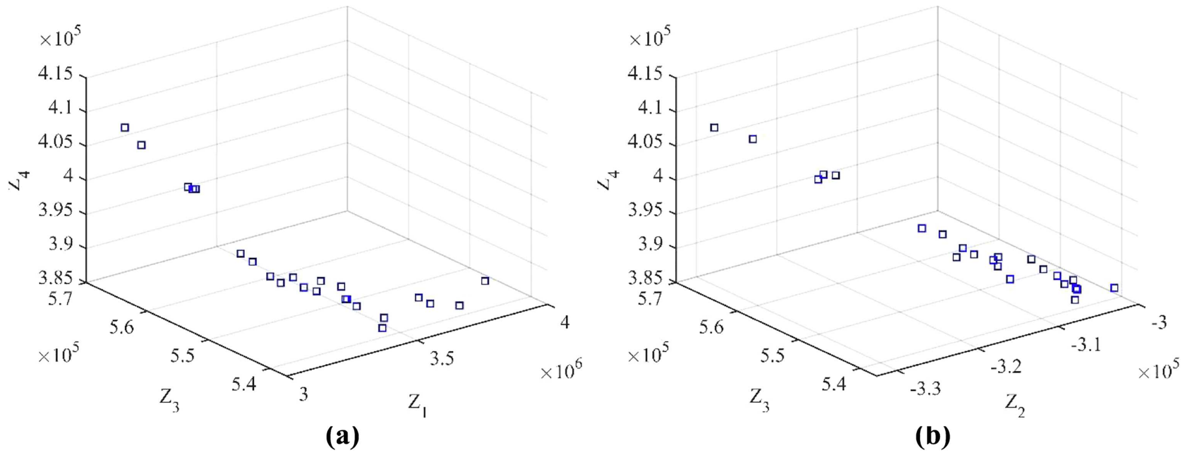


FIGURE 13. Pareto front solution in three-dimensional space: (a) cost-environmental-resilience, (b) social-environmental-resilience.

the supply chain's performance. For instance, resilience strategies improved the network's robustness against disruptions by up to 40% individually and 60% when integrated.
- The high costs of establishing new warehouses in provinces significantly impact distributors' decisions. To encourage the establishment of these provincial warehouses, the government could provide construction loans. This would not only increase resilience but also ensure continuity in drug distribution.
- Since fortifying costs did not significantly reduce distributors' operational efficiency and fortification of facilities contributed the most to improving resilience, the government can shape mandatory policies towards equipping distributors' warehouses in line with its goals.

By integrating these insights into their supply chain management practices, managers can build a more resilient, sustainable, and efficient pharmaceutical supply chain network capable of withstanding disruptions and meeting demands.

6. Conclusion

This paper proposes a multi-objective and multi-time period nonlinear mathematical model to design a PSC network under the perishability of medicine. The vulnerability of the pharmaceutical supply chain to disruption, especially in MCs, results in product flow stoppage, and consequently, it costs human lives in the COVID-19 situation. To this end and to fulfil the gap in the literature, we integrated three main categories of resilience strategies, namely (I) supply and demand management strategies, (II) network complexity management strategies, and (III) inventory management strategies to mitigate the negative impacts of disruption through enhancing the network resilience level. On the other hand, TBL of sustainability has been considered by growing the consciousness toward environmental and social issues. Thus, four objective functions aim to (1) minimize total network cost, (2) maximize the social indicators, (3) minimize CO_2 emission, and (4) minimize de-resilience measures simultaneously. Lexicographic goal programming has also been employed to solve the multi-objective model as an exact solution method for small-scale and medium-scale problems.

The results of this research can help the Food and Drug Organization, government, and managers to make appropriate decisions in the PSC network. To show the capabilities of the proposed PSC model and its effective implementation in a real situation, sets of input parameters for a case study in Iran have been used. Due to the NP-hard nature of the proposed model in a large-scale problem such as the mentioned case study problem, NSGA-II, as an evolutionary algorithm, has been implemented to solve the multi-objective model efficiently.

Furthermore, according to the comparison between the results of the resilient model type, the superiority of the fully resilient model over the other ones has ultimately been proven. Also, the effects of changing some critical parameters on objective functions were investigated, and based on the results, an increase in strategic stock was beneficial. Eventually, a set of Pareto front solutions was provided to show trade-off relationships between the respective objective functions.

This research advances current knowledge by using the NSGA-II algorithm to optimize pharmaceutical supply chains, considering perishability, across four objectives: cost, social impact, environmental sustainability, and resilience. Unlike previous studies that often focus on fewer objectives, our work integrates various resilience strategies and provides a comprehensive framework addressing these critical aspects simultaneously. This holistic approach to decision-making in supply chain management extends the literature with a multi-dimensional perspective that aligns with broader sustainability and resilience goals.

Although important insights have resulted from implementing the proposed PSC model, our study is not without limitations that can be resolved in future research. For instance, in this model, the uncertainty of parameters has been overlooked and assumed deterministic. Future research can address this limitation by applying effective approaches to dealing with uncertainties, such as stochastic, fuzzy, and robust programming, or even integrating them as a hybrid approach. A critical direction can be a closer look at COVID-19, such as viral infection features, pharmaceutical specifications, etc. Also, applying another exact or heuristic solution method can be another good direction for further research due to increased computation time.

Appendix A.

In order to run the test problem (see Tab. 3) coded in GAMS, the parameters are gathered in Table A.1. Moreover, Table A.2 shows the distances between case study cities used to compute transportation cost parameters.

TABLE A.1. Range of uniform distributions for generating parameters of test problems.

Parameter	Value	Parameter	Value	Parameter	Value
ec_i	$U \sim [450, 750]$	cc'_i	$U \sim [4.5, 6.5]^{\mathrm{a}}$	ti''_{jkm}	$U \sim [0.1, 0.3]$
ec'_j	$U \sim [30, 60]$	cp_{il}	$U \sim [0.4, 1.1]$	ti'''_{khm}	$U \sim [0.1, 0.3]$
ec''_k	$U \sim [20, 30]$	cs_{il}	$U \sim [0.2, 0.4]$	$ti^{(4)}_{idm}$	$U \sim [0.1, 0.3]$
ec'''_d	$U \sim [30, 40]$	jo_i	$U \sim [450, 950]$	$ti^{(5)}_{jdm}$	$U \sim [0.1, 0.3]$
pc_{pil}	$U \sim [40, 60]$	jo'_j	$U \sim [90, 160]$	$ti^{(6)}_{kdm}$	$U \sim [0.1, 0.3]$
tc_{ijm}	$U \sim [2, 4]^{\mathrm{a}}$	jo''_k	$U \sim [40, 160]$	α	$U \sim [40, 60]$
tc'_{ikm}	$U \sim [2, 4]^{\mathrm{a}}$	jo'''_d	$U \sim [30, 90]$	α'	$U \sim [30, 50]$
tc''_{jkm}	$U \sim [2, 4]^{\mathrm{a}}$	unr_i	$U \sim [0.3, 0.6]$	α''	$U \sim [30, 50]$
tc'''_{khm}	$U \sim [2, 4]^{\mathrm{a}}$	unr'_j	$U \sim [0.3, 0.6]$	α'''	$U \sim [30, 70]$
$tc^{(4)}_{idm}$	$U \sim [0.8, 6]^{\mathrm{a}}$	unr''_k	$U \sim [0.3, 0.6]$	ξ	$U \sim [3, 9]$
$tc^{(5)}_{jdm}$	$U \sim [0.8, 6]^{\mathrm{a}}$	unr'''_d	$U \sim [0.3, 0.6]$	τ	$U \sim [0.2, 0.8]$
$tc^{(6)}_{kdm}$	$U \sim [0.8, 6]^{\mathrm{a}}$	$re\nu_i$	$U \sim [0.5, 1.5]$	ϑ'_{pj}	$U \sim [2, 5]$
cd_{dp}	$U \sim [50, 150]^{\mathrm{a}}$	$re\nu'_j$	$U \sim [0.3, 0.4]$	ϑ''_{pk}	$U \sim [2, 5]$
λ^t_p	$U \sim [0, 0.4]$	$re\nu''_k$	$U \sim [0.1, 0.2]$	cap_i	$U \sim [1, 2]^{\mathrm{b}}$
λ'^t_p	$U \sim [0.1, 0.5]$	$re\nu'''_d$	$U \sim [0.05, 0.1]$	cap'_j	$U \sim [3, 5]^{\mathrm{b}}$
λ''^t_p	$U \sim [0.3, 0.7]$	rdf_i	$U \sim [0.4, 0.7]$	cap''_k	$U \sim [1, 2]^{\mathrm{b}}$
δ_{pd}	$U \sim [100, 200]$	rdf'_j	$U \sim [0.4, 0.7]$	θ_{pil}	$U \sim [4, 10]^{\mathrm{b}}$
Δ_d	$U \sim [0.04, 0.1]^{\mathrm{b}}$	rdf''_k	$U \sim [0.4, 0.7]$	D^t_{ph}	$U \sim [1.5, 3.5]^{\mathrm{b}}$
hc_{pi}	$U \sim [10, 15]^{\mathrm{a}}$	rdf'''_d	$U \sim [0.1, 0.3]$	φ^t_l	$U \sim [0.1, 0.8]$
hc'_{pj}	$U \sim [10, 15]^{\mathrm{a}}$	set_{il}	$U \sim [5, 7]$	pd^t_{il}	$U \sim [0.2, 0.8]$
hc''_{pk}	$U \sim [10, 15]^{\mathrm{a}}$	$pef'^t_{pil}(.)$	$U \sim [0.5, 1]$	ae^t_i	$U \sim [500, 1500]$
hc'''_{dp}	$U \sim [600, 800]^{\mathrm{a}}$	$de''^t_{pd}(.)$	$U \sim [2, 4]$	ae'^t_d	$U \sim [500, 1500]$
$Emghc'_{pj}$	$U \sim [10, 11]$	ti_{ijm}	$U \sim [0.1, 0.3]$	$ncc^{-\max}_i$	$U \sim [200, 300]$
$Emghc''_{pk}$	$U \sim [10, 11]$	ti'_{ikm}	$U \sim [0.1, 0.3]$	$ncc^{+\max}_i$	$U \sim [200, 300]$
cc_i	$U \sim [1.5, 4.5]^{\mathrm{a}}$				

Notes. [(a)]Parameters are multiplied by 10^{-6}. [(b)]Parameters are multiplied by 10^5.

TABLE A.2. *Distances between cities (km).*

City ID	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
1	0	322	771	868	1007	1047	333	811	387	334	319	545	810	366	243	1148	564	422	668	471	709	644	234	415	783	549	768	286	542	1185	596
2	322	0	479	993	894	785	580	528	133	306	244	227	814	243	140	930	244	125	355	281	411	376	225	566	538	238	566	420	500	1172	307
3	771	479	0	1438	1154	798	1058	564	384	540	693	360	1197	451	530	1020	267	463	156	346	461	542	699	1037	176	397	293	895	896	1512	176
4	868	993	1438	0	692	1148	569	1087	1124	1186	752	1084	353	1184	1033	1061	1171	976	1286	1262	1086	972	774	455	1528	1052	1558	599	555	517	1285
5	1007	894	1154	692	0	540	909	621	1011	1192	706	824	352	1137	1013	385	924	796	1004	1157	697	615	785	732	1305	782	1385	762	468	406	1068
6	1047	785	798	1148	540	0	1121	265	845	1074	743	594	800	988	925	237	665	660	685	955	392	410	821	981	972	563	1080	923	677	945	790
7	333	580	1058	569	909	1121	0	938	684	667	417	763	621	693	555	1155	815	631	932	793	870	773	373	179	1097	750	1094	202	470	974	885
8	811	528	564	1087	621	265	938	0	581	810	530	329	769	724	667	461	402	404	434	690	127	169	599	823	732	299	833	735	550	1011	532
9	387	133	384	1124	1011	845	684	581	0	232	377	252	946	143	147	1013	212	217	292	149	455	452	351	690	415	282	435	542	632	1302	208
10	334	306	540	1186	1192	1074	667	810	232	0	501	484	1072	96	180	1233	438	425	496	194	686	673	439	731	494	511	452	588	767	1442	386
11	319	244	693	752	706	743	417	530	377	501	0	359	576	466	323	830	430	233	549	523	453	362	84	348	776	339	810	221	267	942	534
12	545	227	360	1084	824	594	763	329	252	484	359	0	838	395	355	772	101	133	204	366	203	219	390	707	487	42	561	577	537	1161	244
13	810	814	1197	353	352	800	621	769	946	1072	576	838	0	1042	897	709	935	757	1041	1095	791	682	632	444	1316	800	1369	528	314	375	1067
14	366	243	451	1184	1137	988	693	724	143	96	466	395	1042	0	150	1155	344	351	400	111	598	593	416	734	424	425	402	587	731	1407	292
15	243	140	530	1033	1013	925	555	667	147	180	323	355	897	150	0	1069	344	265	436	238	548	516	267	585	543	373	541	437	590	1265	354
16	1148	930	1020	1061	385	237	1155	461	1013	1233	830	772	709	1155	1069	0	857	808	895	1138	583	562	914	993	1191	736	1294	970	686	768	991
17	564	244	267	1171	924	665	815	402	212	438	430	101	935	344	344	857	0	198	119	291	275	315	446	777	386	143	461	640	630	1262	144
18	422	125	463	976	796	660	631	404	217	425	233	133	757	351	265	808	198	0	316	361	291	251	257	581	561	127	613	447	445	1100	313
19	668	355	156	1286	1004	685	932	434	292	496	549	204	1041	400	436	895	119	316	0	318	319	390	563	896	303	241	399	758	741	1357	119
20	471	281	346	1262	1157	955	793	690	149	194	523	366	1095	111	238	1138	291	361	318	0	563	580	488	819	314	403	302	671	781	1451	201
21	709	411	461	1086	697	392	870	127	455	686	453	203	791	598	548	583	275	291	319	563	0	114	512	775	622	176	717	669	533	1070	409
22	644	376	542	972	615	410	773	169	452	673	362	219	682	593	516	562	315	251	390	580	114	0	430	668	690	179	774	571	419	973	458
23	234	225	699	774	785	821	373	599	351	439	84	390	632	416	267	914	446	257	563	488	512	430	0	341	763	378	785	197	333	1004	531
24	415	566	1037	455	732	981	179	823	690	731	348	707	444	734	585	993	777	581	896	819	775	668	341	0	1103	684	1120	149	309	806	871
25	783	538	176	1528	1305	972	1097	732	415	494	776	487	1316	424	543	1191	386	561	303	314	622	690	763	1103	0	528	122	956	1006	1647	249
26	549	238	397	1052	782	563	750	299	282	511	339	42	800	425	373	736	143	127	241	403	176	179	378	684	528	0	603	559	502	1120	286
27	768	566	293	1558	1385	1080	1094	833	435	452	810	561	1369	402	541	1294	461	613	399	302	717	774	785	1120	122	603	0	972	1056	1712	317
28	286	420	895	599	762	923	202	735	542	588	221	577	528	587	437	970	640	447	758	671	669	571	197	149	956	559	972	0	297	902	727
29	542	500	896	555	468	677	470	550	632	767	267	537	314	731	590	686	630	445	741	781	533	419	333	309	1006	502	1056	297	0	676	758
30	1185	1172	1512	517	406	945	974	1011	1302	1442	942	1161	375	1407	1265	768	1262	1100	1357	1451	1070	973	1004	806	1647	1120	1712	902	676	0	1401
31	596	307	176	1285	1068	790	885	532	208	386	534	244	1067	292	354	991	144	313	119	201	409	458	531	871	249	286	317	727	758	1401	0

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References

[1] C. Aschwanden, Five reasons why COVID herd immunity is probably impossible. *Nature* **591** (2021) 520–522.
[2] S.K. Paul and P. Chowdhury, A production recovery plan in manufacturing supply chains for a high-demand item during COVID-19. *Int. J. Phys. Distrib. Logist. Manag.* **51** (2020) 104–125.
[3] S.A. Melnyk, D.J. Closs, S.E. Griffis, C.W. Zobel and J.R. Macdonald, Understanding supply chain resilience. *Supply Chain Manag. Rev.* (2014) 34–41.
[4] S.I. Mari, Y.H. Lee and M.S. Memon, Sustainable and resilient supply chain network design under disruption risks. *Sustainability* **6** (2014) 6666–6686.
[5] M. Roshan, R. Tavakkoli-Moghaddam and Y. Rahimi, A two-stage approach to agile pharmaceutical supply chain management with product substitutability in crises. *Comput. Chem. Eng.* **127** (2019) 200–217.
[6] B. Zahiri, P. Jula and R. Tavakkoli-Moghaddam, Design of a pharmaceutical supply chain network under uncertainty considering perishability and substitutability of products. *Inf. Sci.* **423** (2018) 257–283.
[7] M. Zhalechian, R. Tavakkoli-Moghaddam, B. Zahiri and M. Mohammadi, Sustainable design of a closed-loop location-routing-inventory supply chain network under mixed uncertainty. *Transp. Res. E* **89** (2016) 18–214.
[8] M. Sherafati, M. Bashiri, R. Tavakkoli-Moghaddam and M.S. Pishvaee, Supply chain network design considering sustainable development paradigm: a case study in cable industry. *J. Clean. Prod.* **234** (2019) 366–380.
[9] Z. Mohammadian-Behbahani, A. Jabbarzadeh and M.S. Pishvaee, A robust optimization model for sustainable blood supply chain network design under uncertainty. *Int. J. Ind. Syst. Eng.* **31** (2019) 475–494.
[10] J. Jouzdani and K. Govindan, On the sustainable perishable food supply chain network design: A dairy products case to achieve sustainable development goals. *J. Clean. Prod.* **278** (2020) 123060.
[11] E. Babaee Tirkolaee, A. Goli, P. Ghasemi and F. Fariba Goodarzian, Designing a sustainable closed-loop supply chain network of face masks during the COVID-19 pandemic: pareto-based algorithms. *J. Clean. Prod.* **333** (2022) 130056.
[12] M. Azani, M. Shaerpour, M.A. Yazdani, M. Azani, M. Shaerpour, M.A. Yazdani, A. Aghsami and F. Jolai, A novel scenario-based bi-objective optimization model for sustainable food supply chain during the COVID-19: a case study. *Process Integr. Optim. Sustain.* **6** (2022) 13–159.
[13] A. Lotfi, M. Shakouri, S.R. Abazari, A. Aghsami and M. Rabbani, A multi-objective optimization for a closed-loop sustainable pharmaceutical supply chain network design: a case study. *J. Adv. Manag. Res.* **20** (2023) 565–598.
[14] S.A. Torabi, M. Baghersad and S.A. Mansouri, Resilient supplier selection and order allocation under operational and disruption risks. *Transp. Res. E* **79** (2015) 22–48.
[15] F. Sabouhi, M.S. Pishvaee and M.S. Jabalameli, Resilient supply chain design under operational and disruption risks considering quantity discount: a case study of pharmaceutical supply chain. *Comput. Ind. Eng.* **126** (2018) 657–672.
[16] A. Diabat, A. Jabbarzadeh and A. Khosrojerdi, A perishable product supply chain network design problem with reliability and disruption considerations. *Int. J. Prod. Econ.* **212** (2019) 125–138.
[17] S.M. Gholami-Zanjani, W. Klibi, M.S. Jabalameli and M.S. Pishvaee, The design of resilient food supply chain networks prone to epidemic disruptions. *Int. J. Prod. Econ.* **233** (2021) 108001.
[18] R. Rajabi, E. Shadkam and S.M. Khalili, Design and optimization of a pharmaceutical supply chain network under COVID-19 pandemic disruption. *Sustain. Oper. Comput.* **5** (2024) 102–111.
[19] B. Fahimnia and A. Jabbarzadeh, Marrying supply chain sustainability and resilience: a match made in heaven. *Transp. Res. E* **91** (2016) 306–324.
[20] A. Hasani and A.H. Khosrojerdi, Robust global supply chain network design under disruption and uncertainty considering resilience strategies: a parallel memetic algorithm for a real-life case study. *Transp. Res. E* **87** (2016) 2–52.
[21] S.M. Khalili, F. Jolai and S.A. Torabi, Integrated production–distribution planning in two-echelon systems: a resilience view. *Int. J. Prod. Res.* **55** (2017) 1040–1064.

[22] F. Lücker and R.W. Seifert, Building up resilience in a pharmaceutical supply chain through inventory, dual sourcing and agility capacity. *Omega* **73** (2017) 11–124.
[23] J. Namdar, X. Li, R. Sawhney and N. Pradhan, Supply chain resilience for single and multiple sourcing in the presence of disruption risks. *Int. J. Prod. Res.* **56** (2017) 2339–2360.
[24] S. Rezapour, R. Zanjirani Farahani and M. Pourakbar, Resilient supply chain network design under competition: a case study. *Eur. J. Oper. Res.* **259** (2017) 1017–1035.
[25] A. Ghavamifar, A. Makui and A.A. Taleizadeh, Designing a resilient competitive supply chain network under disruption risks: a real-world application. *Transp. Res. E* **115** (2018) 87–109.
[26] E.L. Tucker, M.S. Daskin, B.V. Sweet and W.J. Hopp, Incentivizing resilient supply chain design to prevent drug shortages: policy analysis using two and multi-stage stochastic programs. *IISE Trans.* **52** (2020) 394–412.
[27] M. Arabi and M.R. Gholamian, Resilient closed-loop supply chain network design considering quality uncertainty: a case study of stone quarries. *Resour. Policy* **80** (2023) 103290.
[28] C.L. Redman, Should sustainability and resilience be combined or remain distinct pursuits? *Ecol. Soc.* **19** (2014) 2.
[29] B. Zahiri, J. Zhuang and M. Mohammadi, Toward an integrated sustainable-resilient supply chain: a pharmaceutical case study. *Transp. Res. E* **103** (2017) 109–142.
[30] A. Jabbarzadeh, B. Fahimnia and F. Sabouhi, Resilient and sustainable supply chain design: sustainability analysis under disruption risks. *Int. J. Prod. Res.* **56** (2018) 5945–5968.
[31] M. Yavari and H. Hamed Zaker, An integrated two-layer network model for designing a resilient green-closed loop supply chain of perishable products under disruption. *J. Clean. Prod.* **230** (2019) 198–218.
[32] A. Haeri, S.M. Hosseini-Motlagh, M.R.G. Samani and M. Rezaei, A mixed resilient-efficient approach toward blood supply chain network design. *Int. Trans. Oper. Res.* **27** (2020) 1962–2001.
[33] M.M. Vali-Siar and E. Roghanian, Sustainable, resilient and responsive mixed supply chain network design under hybrid uncertainty with considering COVID-19 pandemic disruption. *Sustain. Prod. Consum.* **30** (2022) 278–300.
[34] N. Foroozesh, B. Karimi and S.M. Mousavi, Green-resilient supply chain network design for perishable products considering route risk and horizontal collaboration under robust interval-valued type-2 fuzzy uncertainty: a case study in food industry. *J. Environ. Manag.* **307** (2022) 114470.
[35] M. Rezaei-Malek, R. Tavakkoli-Moghaddam, B. Zahiri and A. Bozorgi-Amiri, An interactive approach for designing a robust disaster relief logistics network with perishable commodities. *Comput. Ind. Eng.* **94** (2016) 201–215.
[36] M.R.G. Samani, S.A. Torabi and S.M. Hosseini-Motlagh, Integrated blood supply chain planning for disaster relief. *Int. J. Disaster Risk Reduct.* **27** (2018) 168–188.
[37] M. Akbarpour, S.A. Torabi and A. Ghavamifar, Designing an integrated pharmaceutical relief chain network under demand uncertainty. *Transp. Res. E* **136** (2020) 101867.
[38] S. Abbasi, A. Saboury and M.S. Jabalameli, Reliable supply chain network design for 3PL providers using consolidation hubs under disruption risks considering product perishability: an application to a pharmaceutical distribution network. *Comput. Ind. Eng.* **152** (2021) 107019.
[39] O. Hashemi-Amiri, F. Ghorbani and R. Ji, Integrated supplier selection, scheduling, and routing problem for perishable product supply chain: a distributionally robust approach. *Comput. Ind. Eng.* **175** (2023) 108845.
[40] F. Shekoohi Tolgari and N.A. Zarrinpoor, Robust reverse pharmaceutical supply chain design considering perishability and sustainable development objectives. *Ann Oper Res.* (2024). DOI: 10.1007/s10479-024-05871-3.
[41] P. Dutta and H. Shrivastava, The design and planning of an integrated supply chain for perishable products under uncertainties: a case study in milk industry. *J. Model. Manag.* **15** (2019) 1301–1337.
[42] P. Mousavi Ahranjani, S.F. Ghaderi, A. Azadeh and R. Babazadeh, Robust design of a sustainable and resilient bioethanol supply chain under operational and disruption risks. *Clean Technol. Environ. Policy* **22** (2020) 119–151.
[43] S.M. Hosseini-Motlagh, M.R.G. Samani and F. Abbasi Saadi, A novel hybrid approach for synchronized development of sustainability and resiliency in the wheat network. *Comput. Electron. Agric.* **168** (2020) 105095.
[44] V.N. Hsu, An economic lot size model for perishable products with age-dependent inventory and backorder costs. *IIE Trans.* **35** (2003) 77–780.
[45] A. Charnes and W.W. Cooper, Management models and industrial applications of linear programming. *Manag. Sci.* **4** (1957) 38–91.
[46] J.P. Ignizio, Goal Programming and Extensions, 1st edition. Lexington Books, The University of Michigan (1976).
[47] G.H. Tzeng and J.J. Huang, Fuzzy Multiple Objective Decision Making, 1st edition. Chapman and Hall/CRC (2019).
[48] M.S. Pishvaee, J. Razmi and S.A. Torabi, An accelerated Benders decomposition algorithm for sustainable supply chain network design under uncertainty: a case study of medical needle and syringe supply chain. *Transp. Res. E* **67** (2014) 1–38.

[49] M. Yavari and M. Geraeli, Heuristic method for robust optimization model for green closed-loop supply chain network design of perishable goods. *J. Clean. Prod.* **226** (2019) 28–305.

[50] M. Mohammadi, F. Jolai and R. Tavakkoli-Moghaddam, Solving a new stochastic multi-mode p-hub covering location problem considering risk by a novel multi-objective algorithm. *Appl. Math. Model.* **37** (2013) 10053–10073.

[51] K. Deb, S. Agrawal, A. Pratap and T. Meyarivan, A fast elitist non-dominated sorting genetic algorithm for multi-objective optimization: NSGA-II, in Parallel Problem Solving from Nature PPSN VI. PPSN 2000. Vol. 1917 of *Lecture Notes in Computer Science*, edited by M. Schoenauer, K. Deb, G. Rudolph, X. Yao, E. Lutton, J.J. Merelo and H.-P. Schwefel. Springer (2000).

[52] Z. Michalewicz, Genetic Algorithms + Data Structures = Evolution Programs, 3rd edition. Springer, Berlin (1996)

[53] D.E. Goldberg and J.H. Holland, Genetic algorithms and machine learning. *Mach. Learn.* **3** (1988) 95–99.

[54] M. Jaberidoost, L. Olfat, A. Hosseini, A. Kebriaeezadeh, M. Abdollahi, M. Alaeddini and R. Dinarvand, Pharmaceutical supply chain risk assessment in Iran using analytic hierarchy process (AHP) and simple additive weighting (SAW) methods. *J. Pharm. Policy Pract.* **8** (2015) 9.

[55] G. Abdollahzade and A. Sharifzadeh, Classifying regional development in Iran (application of composite index approach). *Urban-Reg. Stud. Res. (Univ. Isfahan)* **4** (2012) 41–62.

[56] R.N. Stavins, Chapter 9 – Experience with market-based environmental policy instruments, in Handbook of Environmental Economics. Vol. 1 (2003) 355–435.