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Research Article

Simulation of Supply Chain Resilience Model of the Pharmaceutical Industry in the Country in the Supply of Remdesivir Using System Dynamics Approach

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Abstract

Background: In the event of a crisis and epidemic of infectious disease, ensuring the proper and timely supply of necessary medicine is one of the main priorities of the health care system in any country. Therefore, the present study investigates the resilience of the Iranian medicine supply chain using the system dynamics simulation method in increasing the level of access to Remdesivir.

Methods: This is a development-applied study to provide a model using the system dynamics approach, which first presents a rich image that is based on the model, and then cause-effect models appropriate to the observations made. It was structured on the behavior of the system and also inspired by valid theories. The effect of key factors affecting the supply chain resilience of the country's pharmaceutical industry was designed and analyzed using a system dynamics approach using decision support system (DSS) Vensim software. The time horizon considered for this research was 5 years, from 2019 to 2023. To predict and simulate the system dynamics model, the data collected from the questionnaires and the interviews with experts in this field were used.

Results: Based on the result of this study, it can be expected that by reducing the schedule pressure by 1 and 3 % during the time of the study, the resilience of the supply chain of remedesvir in the country upgraded to about 32% and 47%.

Conclusions: According to the complexity of health care systems, it is difficult to recognize the interaction of different variables, therefore, the effect of interventions is not immediately recognizable and requires the passage of time. In addition, the majority of the factors influencing health care outcomes are nonlinear. Therefore, the use of simulation models can help to clarify the indirect behavior of complex health care problems.

Keywords: Simulation, Chain Resilience, Pharmaceutical Industry, Remdesivir, Resilience, System Dynamics Approach

1. Background

In the event of a crisis and epidemic of infectious disease, ensuring the proper and timely supply of necessitate medicine is one of the main priorities of the health care system in any country (1).

The pharmaceutical supply chain means the route through which high-quality pharmaceutical products are distributed to end-users at the right place and time (2). The Covid-19 pandemic has caused long-term vulnerabilities in the medical supply chain, including medicine supply (1, 3), and the resilience of this chain has faced new challenges during the crisis.

Over the last two decades, the complexity of the business environment, dynamism, uncertainty, and higher environmental fluctuations, concepts such as globalization and increased competition, have led to many changes in the equations governing the supply chain of industries. Under such circumstances, businesses must prepare for the constant flow of challenges such as economic crises, sanctions, exchange rate, and price fluctuations, production system constraints, or natural disasters. "Resilience" is one of the strategies to deal with such challenges (4).

A flexible supply chain can recover from the negative effects of unknown disturbances and adapt to uncertain future events. While there are several definitions of resilience in the literature, the definition of the National Academy of Sciences (NAS) takes the most comprehensive and comprehensive approach to defining resilience and its quantitative modeling. According to NAS, resilience is "the ability to prepare and plan, absorb, improve and further adaptation to adverse events" (5).

Remedesvir is one of the most widely used medicines in the treatment of Covid-19, which is approved by the US Food and Drug Administration (FDA) for adult patients and hospitalized children (over 12 years of age and weighing 40 kg) (6) and prescribing it on time to the patients has a potential impact on their lives. According to the fact, there is the multiplicity of factors affecting the occurrence or non-occurrence of deficiency in the supply of remedesvir, as well as due to the presence of uncertainty elements in the supply chain of the medicine, the use of system dynamics simulation method to predict supply, demand and management Inventory is applicable.

System dynamics models are continuous simulation models using hypothetical relationships between activities and processes. It was developed by Forrester in 1961 and was first used to address the complexity of industrial economic systems and the world's environmental and demographic problems. These models are closely related to the public systems approach and allow modelers to insert qualitative relationships (expressed in quantitative terms). Similar to all simulation models, all results are subject to hypothetical inputs (7).

The use of this method is important in two ways; First, the application of system dynamics allows the symbolic characteristics of the chain such as feedback loops, delays, and nonlinear relationships to be considered, second, the application of this method leads to the development of supply chain management system that responds quickly to the changes of market demand, while it maintains its inventory at a minimum optimal value (8).

2. Objectives

The present study was conducted to investigate the resilience of the Iranian medicine supply chain using the system dynamics simulation method in increasing the level of access to remedesvir.

3. Methods

This is a Simulation and a development-applied study to provide a model using the system dynamics approach, which first presents a rich image that is based on the model, and then cause-effect models appropriate to the observations made. To identify the psychological factors affecting the supply chain of the pharmaceutical industry, the research method of focus groups was used, and a qualitative interview was conducted within a group of 10 experts in this field. To identify the factors affecting the drug supply chain, a library study was conducted. The time horizon considered for this research was 5 years, from 2019 to 2023. Data analysis was done by decision support system (DSS) Vensim software.

For this study, the simultaneous angling scheme was used, and, to provide a template by using the system dynamics approach, initially, a rich image that is the basis of the model was presented. Then the cause-effect models were structured in accordance with the observations which were made on the system behavior and inspired by valid theories derived from the theoretical foundations of research.

In the system dynamics method, first, the relationship between the studied variables in the framework of amplifier loops and equilibrium loops is expressed, and then the general state of the model based on cause and effect relationships is demonstrated.

A sensitivity analysis test was also used to evaluate the sensitivity of the key variables to the change of parameters studied. So, we selected the parameters that directly affect the variables in a certain ratio in a definite range and examined their effects on the variables (9).

To validate the extracted results from the simulated model, some tests were performed. The initial stages of these tests were performed by software, and their explanation was omitted. The following section describes other tests in detail.

3.1. Error Calculation Test

3.1.1. Root Mean Square Percent Error (RMSPE)

In addition to reproducing the pattern behavior to ensure the simulated results, the error of the key variables is also calculated based on the following methods.

Based on this index, the smaller the difference between real and simulated data, the more the simulation results can be trusted. The error rate in this method is calculated based on the following formula.

$$RMSPE = \sqrt{\frac{1}{\theta}\sum_{i=1}^{\theta}\left(\frac{y_{T+i}^{s}-y_{T+i}^{a}}{y_{T+i}^{a}}\right)}{}^{2}*100$$

In the above formula confirms the simulation results of the pattern variable, confirms the actual data. Accordingly, the closer the minimum error rate is to zero, the lower the error rate (10).

3.1.2. Identifying the Root of the Error

Another method for measuring the deviation of simulated values from real data is the U-Theil's (UT) calculation, which is computed based on the following formula.

$$UT=\sqrt{\frac{\frac{1}{\theta}\sum_{i=1}^{\theta}(y_{T+i}^{s}-y_{T+i}^{a})}{\frac{1}{\theta}\sum_{i=1}^{\theta}(y_{T+i}^{s})^{2}+\frac{1}{\theta}\sum_{i=1}^{\theta}(y_{T+i}^{a})^{2}}}$$

3.1.3. Evaluating the Roots of the Error

Given the importance of the error in predicting, recognizing the sources that reduce error validate the result of the model. The roots of the error can be classified into the following three categories.

(1) Baseline error: When the output of the model is not consistent with the data, this error occurs, which is called

systematic error.

(2) Deviation error: when the variances of real data and simulation are very different this error is observed. The root of this error may also be systematic or unsystematic.

(3) Covariance inequality error: When the results of the model and data are not correlated, this error occurs, which is called non-systematic error (Sterman, 2000). The following formula is used to calculate the root of the error.

$$U^m+U^s+U^c=1$$

$$U^m=(\bar{y}^s-\bar{y}^a)^2 /[\frac{1}{\theta}\sum_{i=1}^{\theta}(y_{T+i}^s - y_{T+i}^a)^2]$$

$$U^s= (SDS - SDA)^2/ [\frac{1}{\theta}\sum_{i=1}^{\theta}(y_{T+i}^s - y_{T+i}^a)^2]$$

$$U^c= [2*(1+r)*(SDS*SDA]/ [\frac{1}{\theta}\sum_{i=1}^{\theta}(y_{T+i}^s - y_{T+i}^a)^2]$$

$$[(\bar{y}^s-\bar{y}^a)^2+(SDS-SDA)^2+[2*(1+r)*(SDS*SDA)]]/[\frac{1}{\theta}\sum_{i=1}^{\theta}(y_{T+i}^s - y_{T+i}^a)^2]=1$$

The expression $^{s-}$ $\bar{y}^s-\bar{y}^a$ represents the difference between the mean of the simulation information and the mean of the actual information. In addition, standard deviation simulation) SDS) and standard deviation actual (SDA) represent the standard deviation of the simulated and real data, respectively, and r is the correlation coefficient between these two data.

4. Results

Variables that affected the drug supply chain, based on the results of previous studies, was presented in Table 1. These variables was used for scenarios and simulated models. Each of the symbols L, C, A, and R stands for level variable, constant variable, auxiliary variable, and rate variable, respectively.

Table 1. Introduction of the Variables Used in the Research System Model Based on the Library Study Results

Variables		Variables	
Persian	**Latina**	**Persian**	**Latina**
Reference: Cagliano et al. (11), Mahmoodi et al. (12)		Reference: Sterman (13)	
Desired delivery rate		Schedule pressure	
Component order rate		Reference: Faezipour et al. (14)	
Components on order		Level of complaint	
Desired components on order		Cost of services and resources	
Adjustment for components on order		Level of satisfaction	
Component scrap rate		Reference: Torbati et al. (15)	
		Efficiency	
Scrap rate of damaged components		Customer satisfaction about quality of delivered products	
Scrap rate of components with manufacturing faults		Customer satisfaction of responding to requests	
Scrap rate of components made from defective materials		Customer satisfaction of delivery time	
Supplier delivery delay		Human resources training	
Desired production rate		Advanced technologies in production	
Production rate		Rework and parallel work	
Minimum components preparation		Responding to an instant delivery request	
Shipment rate		Working capital	
Lead time		Profit/income	
Inventory management		Reference: researcher-made	
Nominal production capacity		Supplier loyalty	
Actual production capacity		Debts settlement	
Finished product inventory		Timely payment	

4.1. Key Variables and Cause-and-effect Relationships of Research

According to the theoretical foundations, research background, and effective factors in measuring patients' satisfaction with the medicine supply chain and medicine supply chain resilience, the variables presented in Table 1 have been used in the model of this research. It should be noted that due to the abundance of cause and effect loops in this study, only the main and important loops have been described. In the proposed patterns, R-marked loops are called amplifying loops, and B-marked loops are called equilibrium loops.

B1 Equilibrium loop, which is demonstrated in Figure 1, indicates that the components in the order will change in line with the change in the desired delivery rate. It should be noted that this is due to the delay in delivery and consequently the accumulation of orders in this phase. Regarding this issue, the modification of the components in the order will increase or decrease.

The described change was made to reduce the pressure of the schedule to produce components ordered by loyal business partners more quickly. As a result, it can be expected that the inventory of manufactured products will decrease or increase in proportion to the limited capacity available in each sector. Decreasing or increasing the production capacity will cause an alteration in the actual inventory capacity in this regard.

The described order of products provides the basis for elevating or declining the delay in delivery by the supplier for all received orders. Eventually, with the delivery delay fluctuation by the supplier, the expected delivery rate will alter in line with the changes, or other words, it will increase or decrease.

The R1 amplifier loop is a process similar to that previously mentioned for the B1 equilibrium loop, except that the desired delivery rate is converted according to changes in component ordering time and the duration between initiating and finalizing the production process. In this loop, it is observed that increasing or reducing the delay in delivery by the supplier provides the basis for rising or falling the dissatisfaction of the customers and consequently reducing or (increasing) the ordering rate of the components by them.

As the pressure of the schedule decreases due to the reduction of orders, decline or raising will observe in time between the initiation and finalization of the production process. Consequently, with the realization of this, it can be expected that the desired delivery rate will change consistent with the interchange made. In other words, there is a direct relationship between the initiation and finalization time of product processing and desired delivery rate.

Equilibrium loop B2 which is demonstrated in Figure 2, indicates that the desired delivery rate altered by the component order rate, due to customer satisfaction.

Therefore, the number of orders will change according to the time between the initiation and finalization of the processing period. Regarding this issue provides a basis for reducing or increasing the desired delivery rate for the supplier. Although the R2 amplifier loop follows the same process as in the equilibrium loop B2 until it affects the component ordering rate, this loop changes the desired delivery rate by aligning the components in the order with the ordering rate of the components and then the inverse effect on changing the start and end time of the production process observed.

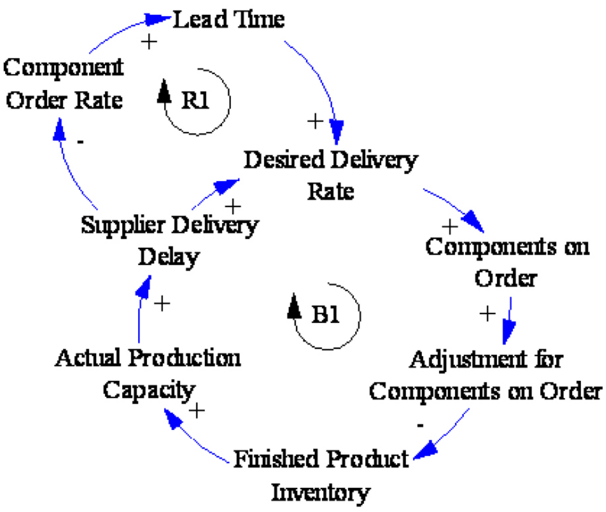


Figure 1. Equilibrium loop and booster of desired delivery rate

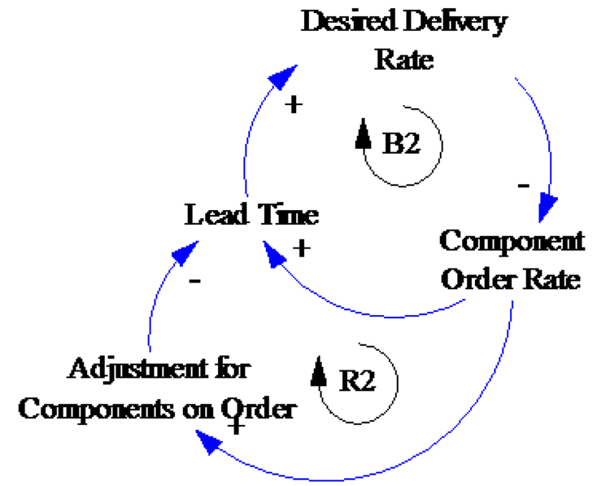


Figure 2. Equilibrium loop and time booster between the initiation and finalization of the production process

Consequently, after reviewing the main loops of the research model, a cause-effect diagram is presented. It should be noted that this is presented in Figure 3

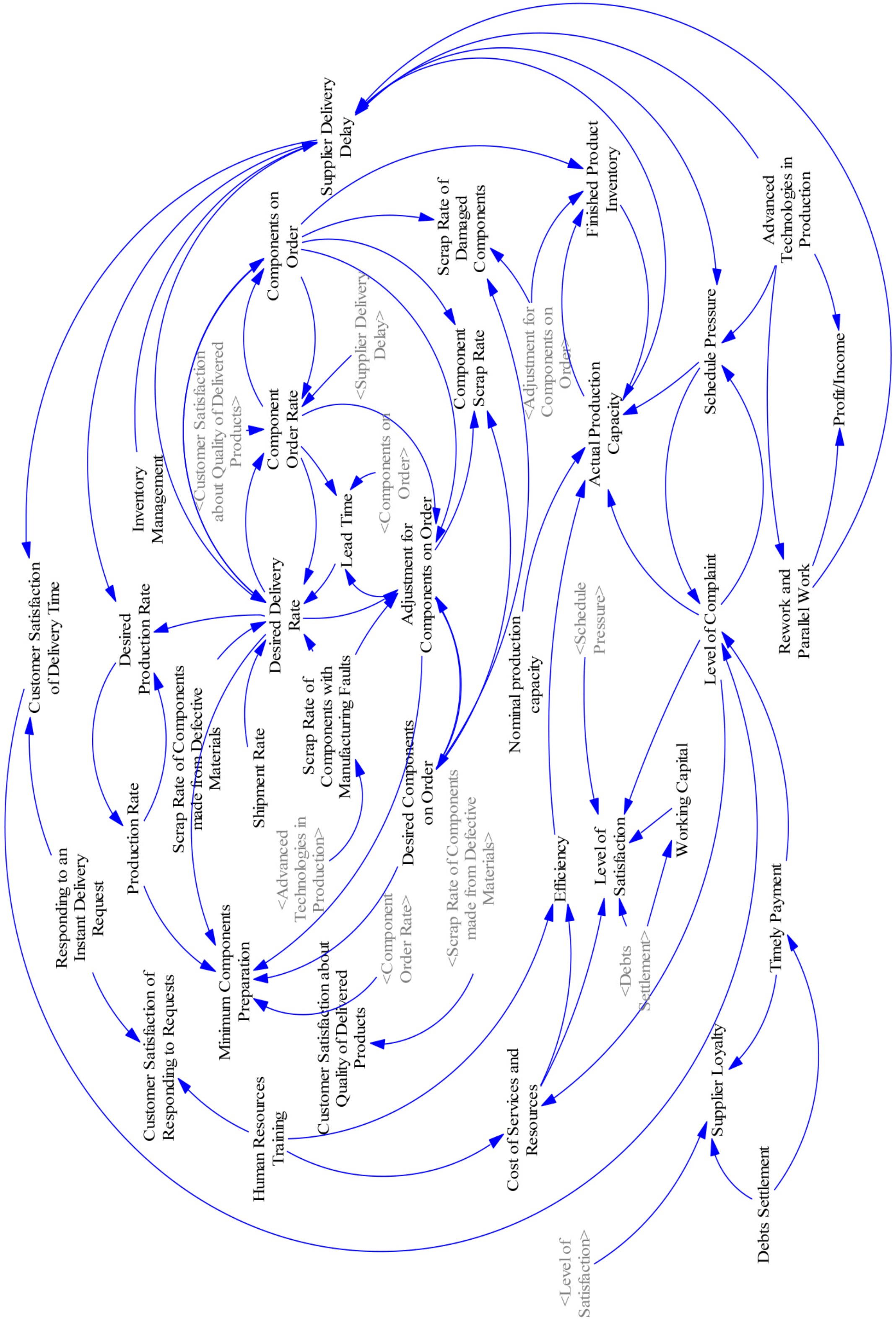


Figure 3. Cause-effect diagrams

Table 2 presents the calculation results of each test and error calculation separately for the key variables studied in the simulation model. Consistent with the results of the error calculation test, it was observed that the minimum squared error for each of the key variables studied is close to zero, which confirms that there is a small error between the simulated data and the real data.

The calculated error rate for each of the key variables of human resource training, inventory management, and cost of resources and services is equal to 0.09110, 0.10173 and 0.0381, respectively. As a result, it can be said that the error rate of the evaluated variables is at the standard level.

Table 2. Error Calculation Test

Cost of Resources and Services	Inventory Management	Human Resource Training	Variables Test
0.08381	0.10173	0.09110	RMSPE
0.05106	0.04511	0.08371	UT
0.16192	0.17441	0.13183	Um
0.28919	0.30118	0.20217	Us
0.5589	0.52440	0.66518	Uc
1	1	1	Um+ Us+ Uc

4.2. Sensitivity Analysis Results

In sensitivity analysis, the sensitivity of patients' level of satisfaction with the medicine supply chain and the resilience of the medicine supply chain to changes in response to the request for immediate delivery were examined. The mentioned parameter was changed by 30% and its effect on the level of patients' satisfaction with the medicine supply chain and resilience of the medicine supply chain was investigated. The results of the sensitivity analysis confirm that a 30% change in response to the immediate delivery request will lead to the medicine supply chain satisfaction with 50, 75, 95 and 100% probability in the yellow, green, blue and gray, respectively (Figure 4).

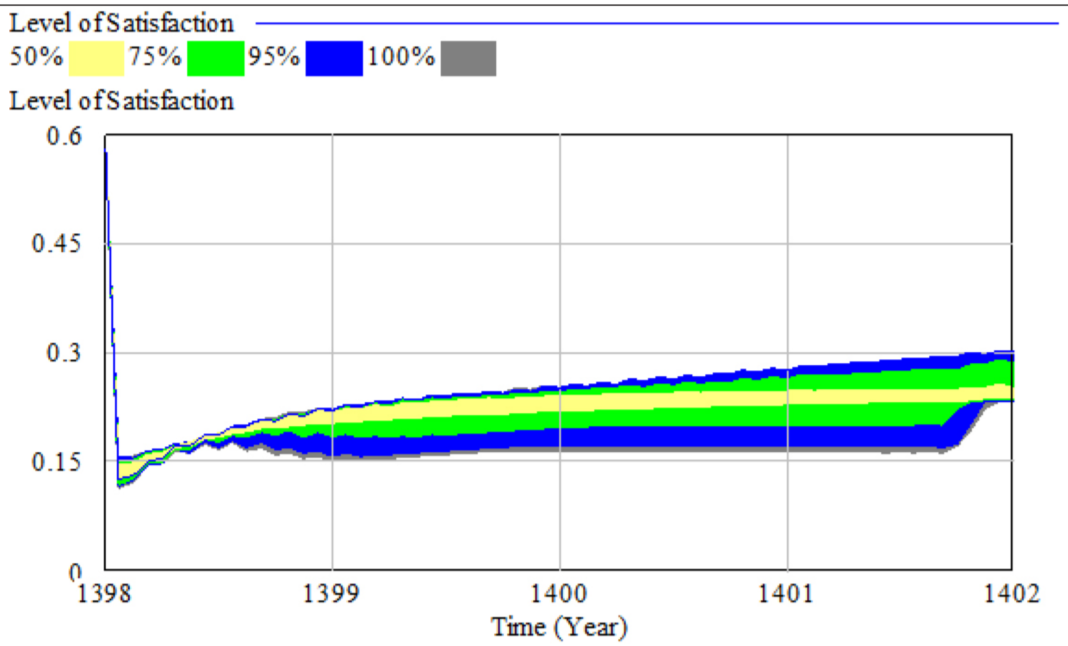


Figure 4. Changes in medicine supply chain resilience

4.3. Behavior Reproduction Test

The purpose of the behavior reproduction test is to compare the simulation results with the available data based on a retrospective view in order to ensure the correct operation of the simulated model (16). The findings in Figure 2 confirm that the actual information and the results of the simulation of the level variable of patients' satisfaction with the supply chain resilience of the medicine supply simulated the behavior of the case variables in the 18-month period (2019 - 2021), well. In the diagrams below, the Level of Satisfaction shown in red confirm the simulated behavior and the Current values shown in blue confirm the actual behavior for the variable (Figure 5).

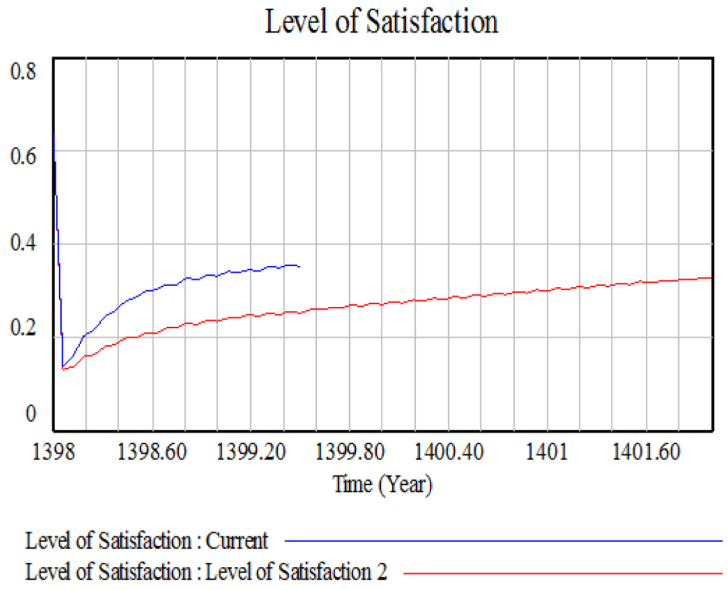
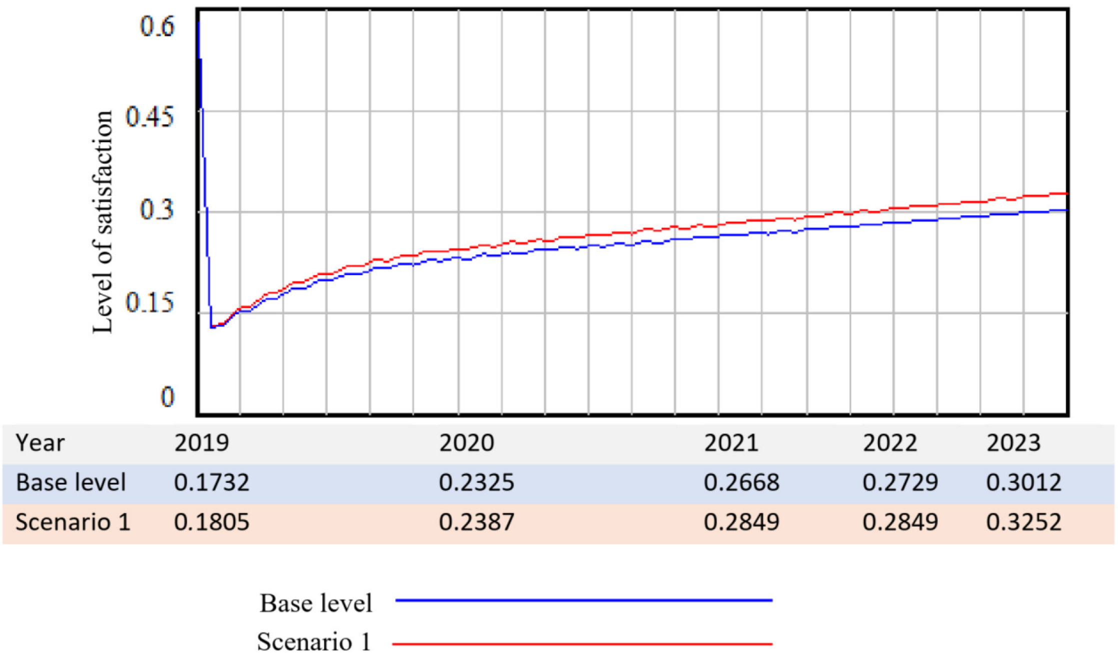


Figure 5. Behavior reproduction test

4.4. Policy-making to Optimize Medicine Supply Chain Satisfaction

Scenario 1: Predicting 1% reduction in schedule pressure during the study period and its effect on patients' satisfaction with medicine supply chain and medicine supply chain resilience.

Based on the simulation results, the implementation of a 1% reduction in schedule pressure provides the reason for increasing the supply chain resilience of the medicine supply chain by an average of about 1.47%. Red line in the presented diagrams confirms the implementation of the studied scenarios (Figure 6).

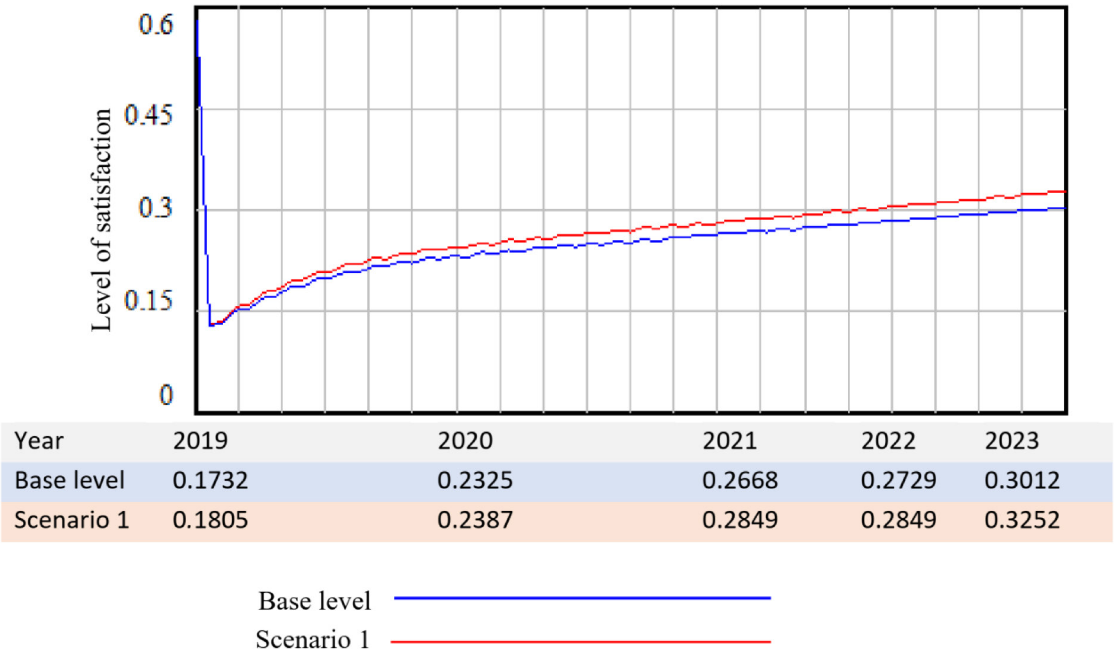


Year	2019	2020	2021	2022	2023
Base level	0.1732	0.2325	0.2668	0.2729	0.3012
Scenario 1	0.1805	0.2387	0.2849	0.2849	0.3252

Figure 6. Impact of 1% reduction in schedule pressure during the period under review and its effect on medicine supply chain resilience.

Scenario 2: Predicting a 3% reduction in schedule pressure during the period under review and its impact on medicine supply chain resilience

Based on the simulation results, the implementation of a 3% reduction in schedule pressure will allow the medicine supply chain resilience to increase by an average of about 11.72% (Figure 7).



Year	2019	2020	2021	2022	2023
Base level	0.1732	0.2325	0.2668	0.2729	0.3012
Scenario 1	0.1805	0.2387	0.2849	0.2849	0.3252

Figure 7. The effect of a 3% reduction in schedule pressure during the period under review and its effect on medicine supply chain resilience

5. Discussion

The global spread of the new coronavirus, also known as the Covid-19 epidemic, has had a devastating effect on supply chains (17). In this study, which investigates the resilience of the Iranian medicine supply chain in reducing the access time to remedesvir, the system dynamics simulation method has been used. However, due to the complexity of health care systems, it is difficult to recognize the interaction of different variables, while the effect of interventions is not immediately recognizable and requires the passage of time (13, 18). Also, many of the factors influencing health care outcomes are nonlinear (19). Therefore, considering these conditions, the use of simulation models can help to clarify the indirect behavior of complex health care problems (20).

It should also be noted that these approaches can lead to deviation of the results due to the linear perspective and not considering the causal relationships between the variables (21). Therefore, in order to address this issue, in the present study, the system dynamics approach has been used. The input variables in this approach are given in Table 1.

In the UK and Greece, it has been shown that the medicine delivery system needs to be improved in terms of quality, visibility, speed and cost to have an effective function (22). The findings of this study indicates that the resilience of the medicine supply chain in 2021 is about 26.68%. According to the increasing trend of this model, it can be expected that the resilience of the medicine supply chain will increase by about 30.12% by the end of the period of study.

In general, it can be said that using the method of simulating system dynamics in order to predict supply and demand and inventory management in times of crisis and ultimately increase the level of access and customer satisfaction of the product is useful. It is also recommended to use this method for other aspects of crisis management, other drugs and with different inputs.

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