

Optimizing Agility in the Pharmaceutical Supply Chain Using Digital Twins to Cope with the Ripple Effect

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Abstract: The pharmaceutical supply chain is a multilayered and complex structure designed to deliver medicines to customers in a timely manner while ensuring optimal quality and quantity of medicines. The COVID-19 outbreak exposed the vulnerability and uncertainty of the pharmaceutical supply chain, so managing the risks in the pharmaceutical supply chain has become particularly important. This study demonstrates that digital twin (DT) technology can improve pharmaceutical supply chain agility and reduce the ripple effect caused by disruptions. The ripple effect refers to the effect that a sudden disruption at one node in the supply chain has on causing a chain reaction in the rest of the supply chain. The most used risk management method today is the Enterprise Resource Planning (ERP) system, which allows for real-time data sharing but has limitations in predicting and modeling the entire supply chain and lacks the ability to make quick decisions and simulate the entire supply chain. DT technology creates a virtual model of the supply chain, which enables continuous communication and information exchange between real assets and the virtual model, offering a promising alternative to risk management for pharmaceutical supply chains. risk management by providing a promising alternative. This study utilizes the AnyLogistix platform to construct a DT model and demonstrates the effectiveness of DT technology in reducing ripple effects and improving supply chain agility using quantitative analysis. This paper focuses on analyzing the pharmaceutical supply chain for 75mg aspirin tablets in London. A supply chain that operates normally, a supply chain that introduces a disruptive event (closure of the logistics center due to an earthquake), and a supply chain that applies a proactive strategy (activation of an alternate logistics center) to mitigate risk are simulated separately. The positive impact of DT technology on the supply chain is evaluated by analyzing the methods of key performance indicators (KPIs) such as inventory level, order fulfillment rate, and delivery time. The experimental results show that DT technology enhances the responsiveness, flexibility, speed, and proactivity of the supply chain, which significantly improves the agility of the supply chain. Proactive and effective strategies also reduce the financial impact of disruptions and service levels are quickly recovered. In addition, the proactive strategy stabilized inventory levels and reduced delayed orders. The above key metrics confirm the hypothesis that DT technology can improve supply chain agility and effectively reduce the ripple effect. Despite the significant conclusions drawn in this paper, there are some limitations. Firstly, sensitivity analysis and t-test were not used in the study for secondary testing, which resulted in the lack of reliability of the validation results. In addition, the possible interaction between the ripple effect and the bullwhip effect was not discussed, leading to a confounding factor in the experimental results. The above issues can be considered in further research in the future. Finally, this paper explores the possibilities and uses of introducing machine learning techniques and considers the supply chain risk factors of globalization. In summary, this study validates the potential of digital twin technology in improving agility and coping with ripple effects in pharmaceutical supply chains. As research continues, DT technology is expected to improve supply chain efficiency and reduce supply chain risk while ensuring patient safety.

Keywords: Pharmaceutical Supply Chain, Digital Twin Technology, Supply Chain Agility, Ripple Effect, Supply Chain Resilience, Simulation Model, Risk Management.

1. Introduction

Medicines are substances that are produced or extracted by means of biotechnology and are used to treat diseases, and access to medicines is one of the most fundamental human rights [1]. Today's pharmaceutical supply chains are multi-linked structures with a high degree of complexity and diversity, which not only need to ensure that medicines have the optimal quality and the right quantity, but also need to be provided to customers in a safe and efficient operational system. The outbreak of COVID-19 in 2019 has brought to light the vulnerability and uncertainty of the pharmaceutical supply chain, and therefore risk management throughout the pharmaceutical supply chain is crucial, identifying, modeling, predicting and making decisions on risky events not only improves shareholders' interests but also ensures the safety of patients' lives [2].

In this context, the pharmaceutical supply chain needs to be proactive in finding solutions to unexpected disruptive

risks. Disruptive events are sudden and uncertain, such as natural disasters, social factors and material shortages [3]. Sudden disruptions can negatively affect specific supply chain nodes and are not limited to a specific area of occurrence but are propagated and spread to other parts of the supply chain creating a ripple effect [4]. This shows that the impact of ripple effect is huge and continuous, which will cause a series of risks and make risk management in the supply chain more difficult. Therefore, it is particularly important to conduct in-depth research and find new methods to solve the ripple effect in the pharmaceutical supply chain.

Nowadays, the more commonly used risk management method is Enterprise Resource Planning (ERP) system, which realizes information sharing within the enterprise and can help the enterprise to optimize and manage the inventory, but the ERP system has limitations in dealing with sudden supply chain disruptions, and it cannot predict and simulate the whole process of the supply chain, and lacks the agility of rapid decision-making and proactive analysis. With the rise of

Industry 4.0 and the Internet of Things (IoT), digital technologies are beginning to be gradually used in supply chain risk management. Digital twin (DT) technology can provide a similar computer simulation model of the actual supply chain, and the physical assets and the virtual model can be bi-directionally connected to each other, which enables continuous communication and information interaction between the two [5]. DT systematically quantitatively analyzes supply chain assets to simulate and predict supply chain behavior and dynamics, and to make short- or medium-term decisions [6]. However, digital twin technology has not yet been extensively used in risk management in pharmaceutical supply chains and is in the research phase but is receiving increasing attention from relevant scholars. In addition, there are fewer works on disruption risk management in pharmaceutical supply chains, and this study is the first attempt to use digital twin technology in disruption risk management in pharmaceutical supply chains and to analyze the effectiveness of digital twin technology on the ripple effect by modeling.

The objective of this study is to utilize digital twin technology in pharmaceutical supply chain to reduce the impact of bullwhip effect on pharmaceutical supply chain by improving the agility of supply chain. In this paper, we use AnyLogistix platform to build a model and quantitatively analyze specific cases to prove that digital twin technology can improve supply chain agility and effectively deal with the ripple effect by analyzing the KPIs in different scenarios.

This paper will demonstrate both qualitatively and quantitatively that digital twin technology can improve the agility of pharmaceutical supply chain and effectively deal with the ripple effect. The literature review section briefly reviews the current state of research on the ripple effect, digital twin technology, agility, and pharmaceutical supply chain, followed by demonstrating the theoretical feasibility of this experiment based on the existing literature and pointing out the shortcomings of the current research. Methodology describes the model design and the experimental design and explains the data sources and hypotheses. In addition, the paper focuses on inputting specific cases and proving the points by analyzing the results of experimental simulations. The Discussion section presents the main insights and research shortcomings of this paper and concludes with an in-depth discussion of future research.

2. Literature Review

2.1. Twin Model Based on Digital Technology

The concept of Industry 4.0 was first introduced by the German government around 2011 with the aim of integrating advanced digital technology frameworks into manufacturing, logistics, and supply chains to achieve higher levels of automation and risk management [7]. With the development of digital technology, it has become a trend to use digital twin technology into supply chains, i.e., transforming physical models of reality into computer models [8]. Digital twin technology was first proposed by Michael Grieves in a presentation there on product lifecycle management and was described as a framework of digital information connected to physical systems [9]. With the definition, attempts were made to explain the concept of digital twin technology, Glaessgen E argued that digital twin technology can reflect and predict the life cycle of a twin product using effective and complete data, sensors, and models [10]. The complete twin technology

framework consists of six layers of framework, the first layer is the physical twin supported by RFID technology, Internet of Things (IoT) sensors and GPS devices that are responsible for reading and collecting real-time data. The second layer is a local data source for uploading information, followed by storing the information in a local database in the third layer and utilizing the IoT gateway interface in the fourth layer for data processing and sharing. The fifth layer stores the pre-processed data into a cloud-based information repository and builds the simulation model in the sixth layer [11]. However, simply building simulation models does not meet the needs of supply chain development, so Strozzi and Ghadge point out that the capabilities of digitization and data analytics can be applied to predict and monitor supply chain contingencies in real time [12]. Sheuly screened 1050 publications on the use of network optimization experiments in digital twin technology and indicated that network optimization experiments can be widely used in digital twin technology, and simulation models based on network optimization experiments can assess risks and provide optimal decision support [13]. Furthermore, the study concluded that network optimization can develop the top-level framework of digital twin technology and enhance the decision-making capability of simulation models.

2.2. Utilizing Digital Twins in the Pharmaceutical Supply Chain and Improving Supply Chain Agility

Digital twin technology, which has been used in many fields to track, predict and model physical assets, is increasingly being used in the healthcare industry and is seen as a revolutionary risk management tool for the pharmaceutical supply chain [14]. With globalization and the development of highly complex and sensitive pharmaceutical supply chains with the risk of inventory build-up and sudden disruptions, the ability to approach 100% product availability has become a great challenge in the pharmaceutical supply chain [15]. As research continues, many researchers have identified improving supply chain agility as a keyway to cope with demand changes and uncertain risk events in complex markets and have subdivided agility into four factors, namely flexibility, responsiveness, speed, and proactivity [16, 17, 18, 19]. Combining the function of agility with digital twin technology reveals a definite link between the two, with EY proposing that digital twins are tools that use real-time data to enable forecasting and decision-making in the supply chain and can increase the sensitivity to perceive and respond to sudden disruptive crises similar to the New Crown outbreak [20]. This paper continues to explore how digital twin technology can enhance the flexibility, responsiveness, speed and proactivity of the supply chain, thus effectively improving the agility of the supply chain. First, Ivanov emphasizes the ability of digital twin technology to rapidly adjust strategies and resource allocation, increasing supply chain agility in the face of sudden and uncertain risks [21]. Second, Tozanli and Saénz argued that digital twin technology can help organizations to quickly deal with supply chain disruptions and thus resume operations by responding to unexpected situations and responding quickly through real-time data monitoring and rapid data processing [22]. In addition, Srari in their study noted that automated processes in twin technology speed up data collection and analysis, thereby increasing the speed of logistics management [23]. Finally, Ivanov mentioned that digital twin technology can

help supply chains identify potential risks and demand changes in advance and take proactive preventive measures using predictive analytics and machine learning [24]. In summary, digital twin technology can effectively improve the agility of the pharmaceutical supply chain by enhancing the flexibility, responsiveness, speed, and proactivity of the supply chain. With globalization and changing market demands, pharmaceutical supply chains must become more agile and resilient to cope with the risks of uncertainty and demand fluctuations.

2.3. Digital Twins Tackle Ripple Effects by Improving Supply Chain Agility

Supply chain agility bridges the gap between digital twin technology and the ripple effect. Supply chain agility is defined as an organization's ability to respond and adapt its strategies quickly to meet customer needs in the face of sudden risks and uncertainties [25]. Supply chain agility can effectively reduce the ripple effects of the supply chain. First, supply chains can have the initiative to predict and identify potential risks in the supply chain and proactively provide effective response solutions, and a forward-looking management approach not only reduces supply chain risks, but also wins the initiative for the enterprise [26]. Secondly, the supply chain needs to respond and adjust quickly after recognizing the risks, responsiveness can help companies to adjust inventory levels quickly, thus ensuring the continuity and reliability of the supply chain [27]. Speed is another key factor in mitigating supply chain risks, sudden disruptions require firms to respond in the shortest possible time to minimize the negative impact and recover from the disaster quickly [28]. Finally, supply chain flexibility in responding to unexpected events can optimize and simulate supply chain configuration requirements, and firms have the flexibility to adjust their response strategies in unexpected situations, thus minimizing losses [29]. Digital twin technology can improve supply chain agility in exactly the four aspects mentioned above, so digital twin technology improves supply chain agility, thus effectively providing solutions and decision support for risky supply chain disruptions.

Most of the literature in the study of utilizing digital twin technology to manage the risk of supply chain focuses on coping with the ripple effect through data analysis (e.g., demand forecasting) and proactive response. The main cause of the ripple effect is the risk of sudden disruptions, such as the BASF plant explosion in Germany in 2016 and the tsunami in Japan in 2011, which led to large disruptions in the supply chain, with a chain reaction occurring like dominoes, directly or indirectly leading to a decrease in the supply chain's financial performance and the stock's return [30,31]. Although such contingencies are overloaded with disruptive factors and irregularities, it has been noted that data analytics and modeling can be used to simulate disruption scenarios in real time and for decision support. In addition, analyzing data demonstrates unique value in predicting future disruption events and recovery of supply chain operations after a disruption [32]. Many organizations wish to utilize the large amount of available supply chain data to predict risks and assess supply chain vulnerabilities, thereby improving supply chain resilience [33]. It follows that digital twin technology can significantly improve supply chain sensitivity to the ripple effect caused by risk disruptions [34].

The ripple effect targets low-frequency but high-impact risk factors, while the bullwhip effect targets high-frequency

but low-impact risk factors, and the ripple effect can be seen as an inverse function of the bullwhip effect [35]. The ripple effect reflects the rapid propagation of localized events through the supply chain network with significant global impacts. In contrast, the bullwhip effect reflects a gradual process of amplification of demand fluctuations across all levels of the supply chain, ultimately leading to greater demand fluctuations at upstream supply chain nodes [3]. Understanding the interrelationship between the two helps to formulate effective and accurate supply chain risk management strategies, thereby enhancing overall risk resistance.

In summary, the existing research literature is small in number and most of the literature studies are based on qualitative analysis and lack of strong data support; however, with the rapid development of digital twin technology and Industry 4.0 technology, future research on applying digital twin technology to the pharmaceutical supply chain will become more and more complete to further reduce the risk of the pharmaceutical supply chain. In addition, according to the support of related literature mentioned above, digital twin technology can theoretically reduce the ripple effect of pharmaceutical supply chain by improving the agility of the supply chain.

3. Methodology: Design and Experimental Design of a Simulated Supply Chain Model Based on Digital Technology

The key to digital twin technology is to provide an exhaustive virtual model of the actual supply chain that can predict and analyze the behavior and dynamics of the supply chain and make proactive decisions. The objective of this paper is to design and develop a digital simulation supply chain model for the pharmaceutical supply chain, thus demonstrating that digital twin technology can improve the agility of the pharmaceutical supply chain and thus effectively deal with the ripple effect.

3.1. Model Design

In this paper, the six-layer digital twin architecture proposed by Redelinghuys is referenced in the design of the simulation model, which focuses on describing how to collect, process, and upload data from a real supply chain to maximize the restoration of the existing supply chain [11]. In addition, this paper introduces the AnyLogistix platform in this architecture to build a digital simulation model. The AnyLogistix® platform is a digital analytics platform developed by Anylogic®, Inc. for supply chains. In studying supply chain risk, most researchers and organizations apply this platform for data analysis, which leads to more significant experimental results. For example, Ivanov used AnyLogistix to analyze the impact of an epidemic on a German food retail supply chain, and Singh used AnyLogistix software in a food supply chain to simulate the risk of disruptions in an Indian food supply chain [36].

3.1.1. Physical twin layer

The physical twin layer is the basis of the simulation modeling and collects physical data from each link in the supply chain in real time through devices such as sensors, RFID technology and GPS positioning. In the pharmaceutical supply chain, the physical twin layer first adds RFID tags to pharmaceutical packages at the upstream of the supply chain,

which contain an antenna that transmits the location of the drug in real time and a chip that stores the information. IoT sensors are then deployed at key nodes, such as logistics centers and hospitals, so that environmental changes and drug quantities can be monitored in real time. Finally, GPS devices installed in the transportation vehicles can track the transportation path and location in real time. The purpose of the physical twin layer is to collect real-time data from all parts of the supply chain in the best possible way, so as to ideally replicate the real supply chain 100% and provide a reliable data base for subsequent analysis and strategy. Given that the technology has not been fully applied to the pharmaceutical supply chain, this paper assumes that the simulation model in the case study is infinitely close to the physical model, and that all data used in the study is collected in real time by devices such as sensors, RFID technology, and GPS positioning.

3.1.2. Local data sources

The purpose of local data sources is to collect and preprocess data from the physical twin layer. In the pharmaceutical supply chain, professionals first cleanse and categorize the data with the goal of ensuring accuracy and consistency. The preprocessed data is then quickly uploaded to a local database via automated spreadsheets (Google Sheets and Python scripts), with automated systems increasing the speed and responsiveness of data uploads. During the preprocessing of the data, the relevant personnel use uniform data formats and standards to ensure that the data is readable and usable. Meanwhile, during the automatic entry and storage process, professionals need to check the completeness and accuracy of the data to ensure the quality of the data in the simulation model.

3.1.3. Local data repositories

The role of the local data repository is to store and manage the collected data. In the pharmaceutical supply chain, this paper uses PostgreSQL as the local data repository, the main reason for using this system is that PostgreSQL allows easy access to external data, for example, the system's Foreign Data Wrappers can integrate data from sensors, RFID and GPS. In addition, the system can save data in real time and back it up regularly, thus ensuring data security and integrity.

3.1.4. IoT gateway interface

The IoT gateway interface is a bridge for transferring local data to the cloud storage layer, a technology that is common on the Internet, such as Ethernet, Wi-Fi and Bluetooth. In pharmaceutical supply chain, it is necessary to consider the transmission speed and distance of IoT gateway interfaces at each key node of the supply chain, in addition, the use of appropriate data transmission protocols can achieve high efficiency and low latency data transmission. In this study, Wi-Fi and MQTT protocols are used as IoT gateway interfaces in the pharmaceutical supply chain because WIFI is suitable for scenarios in which a large amount of data is transmitted, which can meet the large-scale data transmission needs of suppliers, hospitals, and logistics centers. And MQTT can transmit data in real time, which improves the data responsiveness in the upstream of the supply chain. Transportation tools use 4G and CoAP protocols because 4G networks have wide coverage and can ensure network stability for transportation tools. In addition, CoAP protocol enables frequent data transmission during transportation, thus tracking the location and status of medicines in real time and optimizing the distribution path.

3.1.5. Cloud-Based Information Repository

Cloud-Based Information Repository is to utilize cloud computing technology to store the information of local database to the server in the cloud, and the more common cloud storage providers are Azure and Google Cloud. In the pharmaceutical supply chain, this paper adopts AnyLogic Private Cloud as the cloud database for pharmaceutical supply chain management. The main reason is that the simulation model built by AnyLogistix can process and analyze the data from AnyLogic Private Cloud more quickly. Secondly, AnyLogic Private Cloud has high-performance computing power, which can help AnyLogistix preprocess a large amount of data, thus improving the running speed and analyzing ability of the simulation model. Most importantly, AnyLogic Private Cloud can effectively prevent data leakage with a complete data encryption system, which protects the sensitive data of pharmaceutical companies.

3.1.6. Simulation Model

The topmost layer of the framework is to build a simulation model, which aims to simulate the real-world supply chain in the computer so as to visualize the real-world supply chain in the computer, and more intuitively show the operation trajectory of the supply chain and the impact of unexpected risk events. For the pharmaceutical supply chain, this paper inputs supply chain data from the cloud into the AnyLogistix platform, so that a simulated supply chain model is constructed using the AnyLogistix platform. The model receives real-time information from the real supply chain and simulates specific disruptions and demand fluctuations in the supply chain to analyze current and future risks and proactively make optimal decisions.

3.1.7. Introduction of digital technology into simulation models

Digital technology is key to improving supply chain agility, and it serves to analyze and process data in the simulation model to predict disruption risks and make proactive decisions for ripple effects. Digital technology mainly consists of network optimization experiments and comparison experiments. Network optimization experiments can proactively analyze the data in the simulation model and find the optimal solution, including parameter setting and path finding. The purpose of the comparison experiment is to compare the effectiveness of different strategies and actively select the optimal strategy. For the ripple effect, digital technology can analyze the factors that affect the ripple effect in the supply chain, analyze which factors have the greatest effect, and adjust these variables. Since sudden disruption events for the ripple effect are difficult to predict, this study utilizes digital technology to select the most effective proactive and stressful strategies for specific disruption risks, such as for a factory fire, digital technology proactively responds to the event by using lateral transshipment and alternate suppliers. This paper will specifically utilize the AnyLogistix platform to build out a digital simulation model in the case study and use the output to demonstrate the positive impact of digital twin technology on agility and ripple effects.

3.2. Experimental Design and Hypothesis

3.2.1. Experimental Design

The purpose of this experiment is to analyze the effect of digital twin technology in the pharmaceutical supply chain through simulation models and specific cases, mainly analyzing the ability of digital twin technology to cope with

the ripple effect of the supply chain. This experiment is demonstrated through specific cases. First, a simulation model is built and simulates the normal operation of the pharmaceutical supply chain, which includes suppliers, manufacturers, distribution centers and retail terminals. Then, 30 iterations of the experiment are conducted without the risk of sudden disruptions and simulate the normal operation of the supply chain for one year, and key performance indicators (KPIs) such as inventory levels, order fulfillment rates, out-of-stock rates, average lead times, and total costs are recorded. Subsequently, 30 iterations of the simulation are conducted with the introduction of a specific sudden disruption event to record the KPI results of the supply chain after the ripple effect occurs over a one-year period and compare this result with the results of the normally operating supply chain to analyze the change in KPIs of the simulated supply chain after the two events.

Next, network optimization experiments are analyzed for the simulated supply chain that has experienced a disruptive event, and network optimization can screen the best solution strategy for the simulated supply chain. Immediately following the input of strategy parameters for the supply chain with a disruptive risk event, 30 iterations of simulation are conducted and KPI results are output respectively. By analyzing and comparing the key parameters output from the three experiments, it is firstly argued that digital twin technology can improve the agility of supply chains. Secondly, assess whether the proactive strategy is effective in reducing the supply chain ripple effect, thus demonstrating the effectiveness of digital twin technology in reducing the supply chain ripple effect. Through the above experimental design, the effectiveness of digital twin technology in terms of its role in supply chain agility and coping with ripple effects can be verified.

3.2.2. Hypotheses

There are 2 hypotheses established in this paper, hypothesis 1: The simulation supply chain based on digital twin

technology can improve the responsiveness, proactivity, flexibility and speed of the supply chain, thus improving the agility of the supply chain. Hypothesis 2: Digital twin technology can effectively reduce the ripple effect of supply chain.

4. Case Study Description of Pharmaceutical Supply Chain

4.1. Study Area

The research object of this paper is the London region located in the U.K. The U.K. is a key player in the global pharmaceutical industry, with world-leading pharmaceutical companies and advanced medical technology, and London, as the capital of the U.K., has abundant medical resources and well-developed infrastructure. In recent years, through technological innovation and centralized management, London has developed a centralized and multi-layered pharmaceutical supply chain network (e.g., Fig. 1). Suppliers and manufacturers deliver medicines through warehouses or directly to centralized logistics hubs (logistics centers), which are responsible for splitting, repackaging, and distributing medicines to hospitals and pharmacies, allowing for efficient "last mile" distribution, e.g., the consolidation center established in Dartford in 2014 reduces the number of times medicines are delivered to central London hospitals (CHC). The NHS (National Health Service) is the foundation of the UK healthcare system, providing free healthcare to UK citizens, and is a key player in the pharmaceutical supply chain. The main reason for choosing London for this study is that London has a well-established pharmaceutical supply chain network and abundant healthcare resources, which can provide rich data support for studying the ripple effect. In addition, the pharmaceutical supply chain in the London region is representative of the overall development level of the UK, and the results of the study may be equally applicable to other regions in the UK.

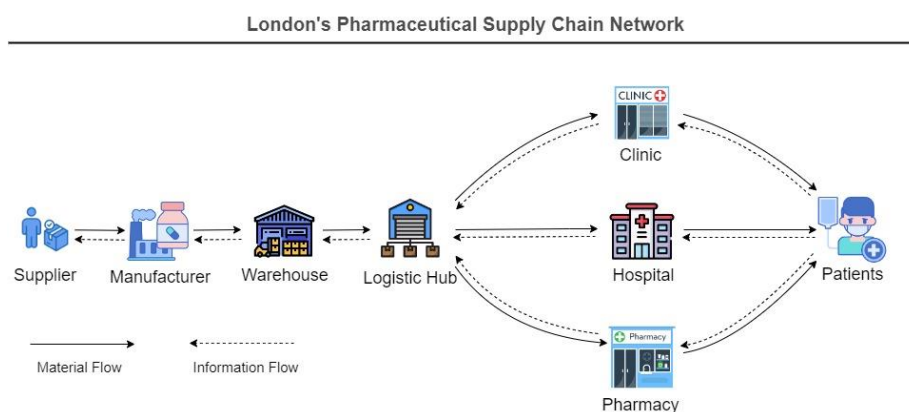


Figure 1. Structure of London's Pharmaceutical Supply Chain Network

4.2. Drug Selection

Due to the variety and huge number of drugs, only 75mg aspirin tablets were selected as the case drug in the pharmaceutical supply chain for this study. Firstly, aspirin has a wide range of applications and a huge demand in the market, with an annual demand of about 30 tons in London, so it is suitable for studying interruption risk events [37]. Secondly, the supply chain of aspirin encompasses the complete pharmaceutical supply chain, covering the entire process from supplier to consumer, so it is suitable for analyzing and

modeling the pharmaceutical supply chain. Finally, aspirin is produced and stored under relatively simple conditions and can be stored at room temperature, which helps to simplify the complex production and transportation processes of the supply chain.

4.3. Study Population

The pharmaceutical supply chain in the London area is extensive and complex, serving approximately 9 million local residents. The pharmaceutical system in London consists of 200 pharmaceutical companies, 150 logistics companies, 70

hospitals, more than 1,300 clinics and 1,800 pharmacies [38]. For this paper, Firstline Pharma was chosen as the supplier in the London area, which has a base of operations in London and can supply imported raw materials to pharmaceutical factories in London. Pfizer has a pharmaceutical factory in the London area that produces aspirin tablets and Pfizer has invested a significant amount of money in London to improve healthcare in London, for example, the vaccine developed in collaboration with BioNTech is widely used in London. Secondly, Alloga UK and Alliance Healthcare were selected as representative pharmaceutical distribution companies (logistics centers), both headquartered in London. Alloga UK has a footprint of approximately 300,000 square meters and can handle over 50,000 pharmaceutical orders per day, specializing in third party logistics (3PL) services for the pharmaceutical and medical device industries. Alliance Healthcare focuses primarily on the London area, with a footprint of approximately 200,000 square feet and the ability to process more than 35,000 pharmaceutical orders per day. Both companies provide efficient logistics services to ensure that medications can be delivered to healthcare facilities quickly. Finally, 15 representative hospitals, 10 clinics and 5 pharmacies were selected for this paper. The data sources for this paper are Alliance Healthcare's internal data and Knowledge Sourcing Intelligence's business reports. Table 1 lists the downstream customers of the pharmaceutical supply chain and the daily demand for 75mg aspirin tablets in this case (Knowledge Sourcing Intelligence, 2022).

This paper specifically examines the four-tier pharmaceutical supply chain for 75mg aspirin tablets in the London area, and Figure 2 illustrates the general process of this supply chain, with Firstline Pharma as the main supplier of raw materials to the Pfizer pharmaceutical plant, and distribution through two pharmaceutical logistics centers, Alliance Healthcare and Alloga UK, to major hospitals, clinics and pharmacies.

Table 1. Daily Demand for 75mg Aspirin Tablets by Hospitals, Clinics, and Pharmacies in London

Table 1 Representative Hospitals, Clinics, and Pharmacies in London and Their Daily Demand for 75mg Aspirin Tablets		
Category	Institution Name	Daily Demand (tablets)
Hospital	St Thomas' Hospital	7,500
Hospital	Royal London Hospital	12,000
Hospital	University College Hospital	9,500
Hospital	King's College Hospital	8,000
Hospital	Chelsea and Westminster Hospital	11,000
Hospital	St George's Hospital	10,500
Hospital	Guy's Hospital	13,000
Hospital	Moorfields Eye Hospital	9,000
Hospital	Great Ormond Street Hospital for Children	7,800
Hospital	Hammersmith Hospital	10,200
Hospital	Homerton University Hospital	11,500
Hospital	Royal Free Hospital	8,700
Hospital	Whipps Cross University Hospital	9,300
Hospital	Charing Cross Hospital	12,500
Hospital	Queen Elizabeth Hospital	8,200
Clinic	Harley Street Clinic	4,000
Clinic	The London Clinic	3,500
Clinic	The Bridge Clinic	4,200
Clinic	The Wellington Clinic	5,000
Clinic	The Medical Chambers Kensington	4,800
Clinic	The Westover Clinic	3,900
Clinic	London General Practice	4,100
Clinic	The Smart Clinics	4,700
Clinic	King Edward VII's Hospital	5,200
Clinic	Fleet Street Clinic	4,500
Pharmacy	Boots (Oxford Street)	2,200
Pharmacy	Superdrug (Strand)	2,500
Pharmacy	LloydsPharmacy (Holborn)	2,700
Pharmacy	Day Lewis Pharmacy (Westminster)	2,300
Pharmacy	John Bell & Croyden (Wigmore Street)	2,600
Total	30	225,000

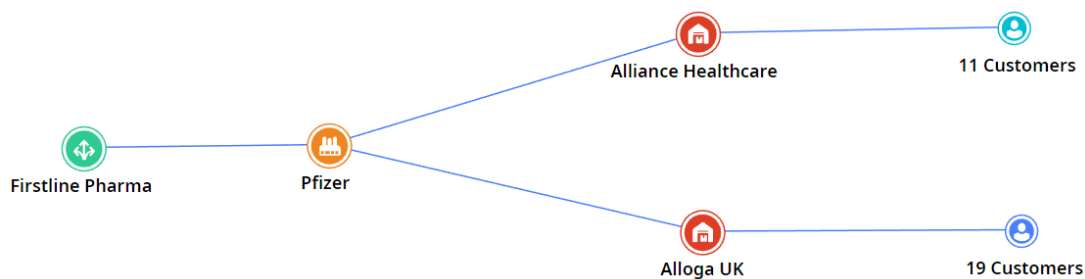


Figure 2. Supply Chain Flow of 75mg Aspirin Tablets

4.4. Model Design

In this paper, we use the AnyLogistix platform to build a simulation model, firstly, we determine the geographic locations of all levels of the supply chain in the simulation model and mark them in the map, with the purpose of visualizing the simulated supply chain and roughly estimating

the distances between the nodes (e.g., Fig. 3). Next, the real-time data from the real supply chain is uploaded to the anyLogic Private Cloud, where the cloud repository preprocesses the data and feeds it into the simulation model. In the end, we built a dynamic simulation of the supply chain for the London region on the AnyLogistix platform.

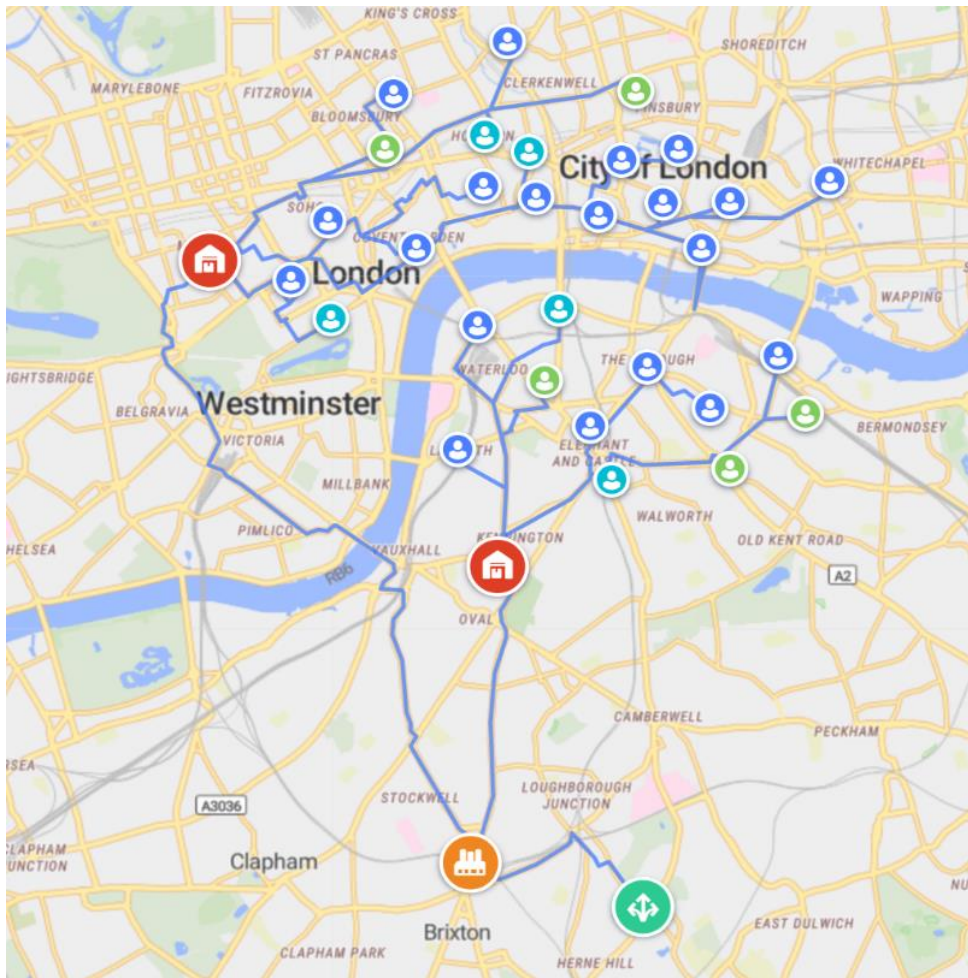


Figure 3. Geographic Visualization of the Supply Chain Network

4.5. Input Data

Firstly, 75mg aspirin was entered as the product in the simulation model and the product was set to sell in London at a price of about £1.50 per packet, each packet contains 28 tablets and costs about £0.56 per packet. Secondly, as aspirin can be stored at room temperature, two types of transportation, truck and rail, were created and transportation configurations were set up for different nodes. In addition, demand and inventory control strategies were set for the case (experimenting with allowing out-of-stock situations so as to assess the supply chain's responsiveness and recovery strategies in the face of contingencies) to ensure proper

inventory management. Finally, appropriate procurement policies are set, and a one-year simulation is set up (January 1, 2023, and December 31, 2023), with detailed input data in see Table A1 in Appendix A.

The simulation model sets up two specific events for the ripple effect, firstly a disruptive event is set up for the ripple effect, a sudden seismic event occurs on the 3rd of July in two logistics centers, Alloga UK and Alliance Healthcare, the distribution centers resulting from this event will need a one month recovery period during which the medications cannot be delivered and after the recovery period is over they will be open again and become operational again after the recovery period. The specific event setup is listed in Table 2.

Table 2. Disruptive Event and Recovery Period Setup in the Simulation Model

Name	Event Type	Parameters	Occurrence Type	Occurrence Time	Trigger	Probability
Logistics Hub Earthquake	Facility state	Object: (Regional DCs), Ne...	Date	7/3/23 6:00 AM	Logistics Hub Earthquake	1
Full Recovery	Facility state	Object: (Regional DCs), Ne...	Delay (days)	30	Logistics Hub Earthquake	1

4.6. Output Results

This experiment records and analyzes the output Key Performance Indicators (KPIs) that validate the effectiveness of digital twin technology in improving agility and reducing ripple effects. To verify that digital twin technology can improve supply chain agility, this experiment utilizes three KPIs to make the argument. First, the order fulfillment rate is utilized to assess the responsiveness of the supply chain in

dealing with unexpected events; the higher number of fulfilled orders indicates the higher responsiveness of the supply chain. Second, the average delivery event per product can be used as an indicator to assess the speed of the supply chain, with shorter delivery times indicating a faster supply chain. Additionally, the amount of inventory that remains available for sale and use in the event of a supply chain disruption is measured; more available inventory indicates a more proactive supply chain. Finally, the flexibility of the

supply chain is judged by measuring the ability of the supply chain to adjust and recover after a disruption.

In order to verify the effectiveness of the ripple effect of the digital twin technology on the supply chain, this experiment chooses five key performance indicators: financial performance, demand processing capability, available inventory (including stockpiled inventory), delayed order quantity and Customer service level. Financial performance can reflect the impact of disruptions on the economic efficiency of the supply chain, and demand handling capacity reflects the supply chain's response speed to changes in demand and replenishment efficiency. Available inventory (including stockpiled inventory) measures the efficiency of the supply chain in managing inventory in the event of a disruption risk, and customer service level reflects whether the customer service level can be unaffected after a sudden disruption risk event. Analyzing the changes in the five metrics assesses the resilience and operational effectiveness of the supply chain, thus demonstrating the effectiveness of the digital twin in dealing with the ripple effect.

5. Experimental Analysis and Results

In this section, we firstly run the simulation of the supply chain in normal state using AnyLogistix platform and output the results, secondly, we simulate the supply chain with disruptions and ripple effects and output the results, and finally, we proactively use the optimal coping strategies for the supply chain with ripple effects and output the results, compare the key KPIs of the three experiments and prove that the digital twin technology can reduce the supply chain's ripple effects.

Similarly, the agility experiment also compares the outputs of the three experiments to demonstrate that the digital twin can improve the agility of the supply chain. Note that repeated experiments are necessary to produce statistically significant results, given that the model contains random parameters. In this paper, the iterative experiments are repeated a total of 300 times with the aim of improving the stability and confidence of the results.

5.1. Validating the Effectiveness of The Digital Twin Technique on The Ripple Effect

5.1.1. Normal State

Figure 4 illustrates the trends and patterns of KPIs in the normal state (without introducing sudden disruptive events). First, the three financial metrics of the aspirin supply chain are proportional to time and show a linear growth trend with time. Second, the service level (ELT Service Level) remained unchanged at 100% over the course of a year, indicating that all products were delivered on time and demonstrated an efficient service capability under normal conditions. In addition, in terms of Demand Processing (DEMAND RECEIVED AND PLACED), although the number of orders processed is lower than the number of orders received, both are proportional to time, and the supply chain is able to process orders efficiently. Importantly, the available inventory level fluctuates regularly between 5 and 45, indicating that the management of inventory is effective in normal conditions and the inventory level shows cyclical variations. Finally, the order fulfillment rate increases steadily over time, indicating that order processing is efficient under normal conditions and the number of delayed orders is almost non-existent.

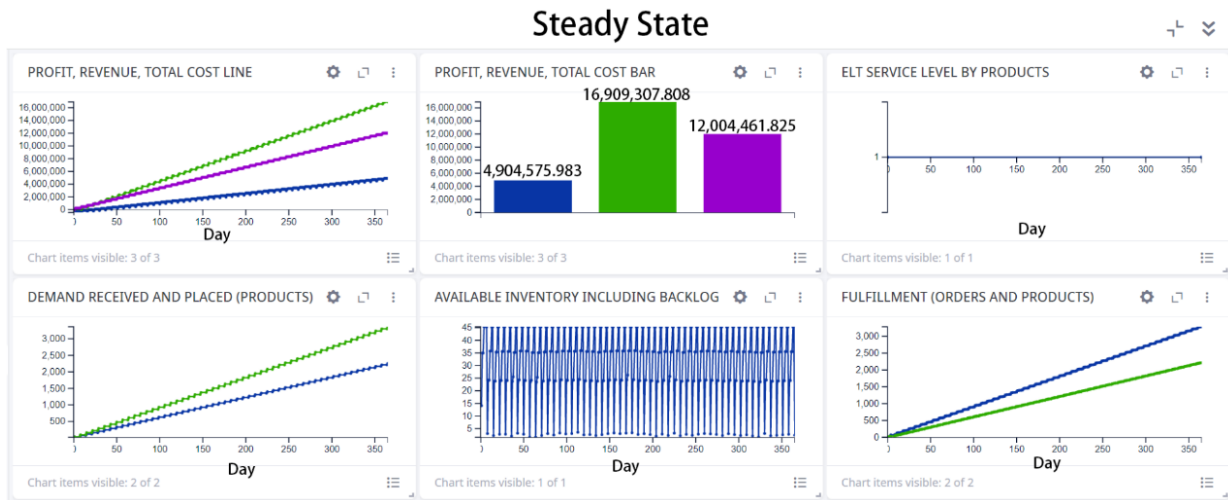


Figure 4. KPI Trends and Performance Metrics in Steady State

5.1.2. Supply chain with ripple effect due to disruption event

Setting up an earthquake event in the logistics center on July 3 in the simulated supply chain, the disruption event resulted in the forced closure of the logistics center, which was reopened only after 1 month, and the event triggered a ripple effect that resulted in damage to both upstream and downstream of the supply chain. Firstly, the disruption event led to a significant reduction in profits and revenues, with profits decreasing by £ 757,152.379 and revenues decreasing by £ 1,162,040.969. Secondly, the service level dropped significantly after being disrupted by the sudden disruptive event, with a low of 87%, and then only gradually

rebounded after the disruptive event was over but was unable to return to 100% service level within a year, and ultimately only 92% service level was reached. In terms of demand processing, the closure of the logistics center resulted in the inability to process and deliver customer orders for a month, so order processing for a month was 0. In addition, available inventory remained at its highest level of around 45 for the month in which the logistics center was closed, suggesting that there was an inventory hold-up problem, which prevented regular fluctuations in available inventory. Finally, in terms of delayed orders and products, the sudden disruption event caused the delayed order volume to grow dramatically to 3,500 orders, and it still took a significant amount of time to

process the delayed orders and products after the logistics center was restored (e.g., Fig. 5).

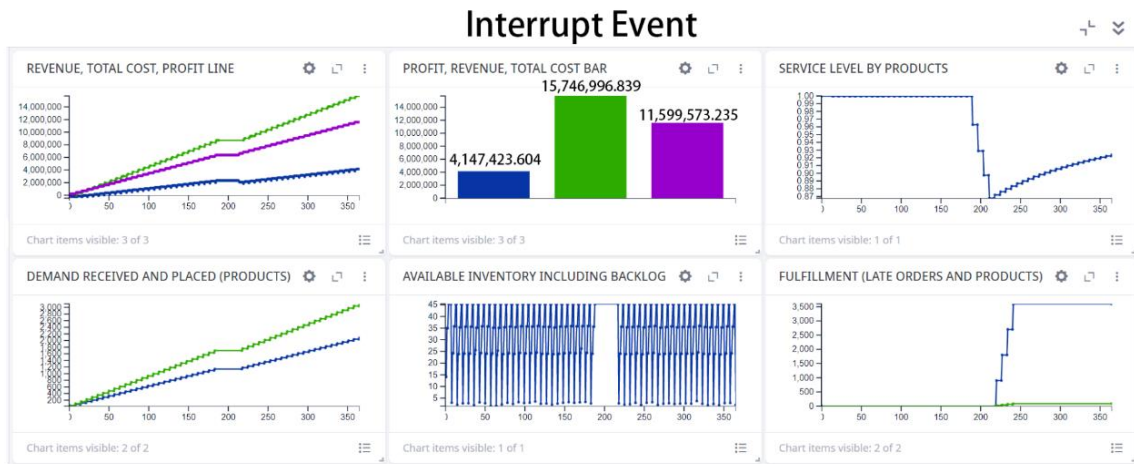


Figure 5. KPI Impact of Disruption Event on Supply Chain Performance

5.1.3. Output results of the simulated supply chain using digital techniques to cope with ripple effects

This study adopts the network optimization technique in digital technology to cope with the ripple effect in the supply chain, which can actively select the optimal strategy for the supply chain to cope with the ripple effect, for this case, the network optimization technique recommends the strategy of activating the alternate logistics center near the closed logistics center, which is not a part of the supply chain, and will only be activated in the case of the forced closure of the logistics center. the alternate logistics center is opened.

The third simulation experiment outputs the results of the simulated supply chain using digital technology (e.g., Fig. 6), and then the outputs of the three simulation experiments are compared using the comparative experiment method. The

comparison is as follows: firstly, the profit after adopting the new strategy only decreased by £ 398,558.505 and the revenue only decreased by £ 427,556.532 (e.g., Fig. 7), which indicates that the new strategy effectively mitigates the financial impacts of disruptions on the supply chain, and effectively controls the ripple effect on the supply chain's financial damage. Secondly, in terms of service level, after using the new strategy, the service level of the supply chain only dropped to 94% and gradually recovered to 96.5% after 1 month, which indicates that the new strategy can timely mitigate the indirect impact of the disruption event on the service level, thus reducing the impact of the ripple effect on the customer service level (e.g., Figure 8).

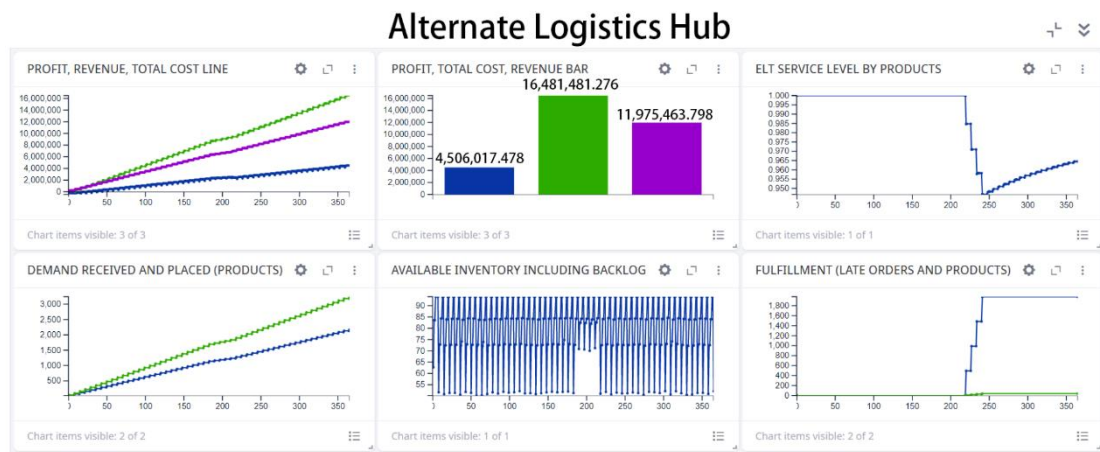


Figure 6. Impact of Alternate Logistics Hub Activation on Supply Chain Performance

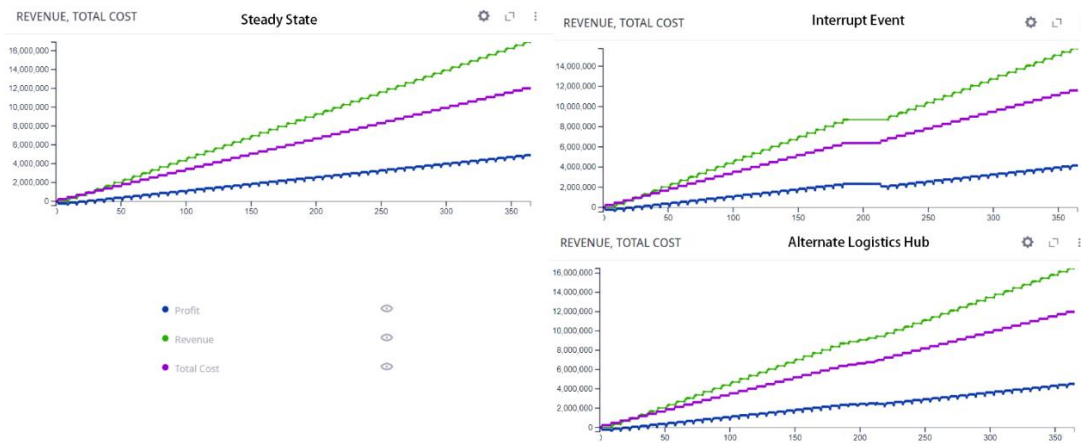


Figure 7. Comparative Analysis of Financial Impact Across Simulation Scenarios

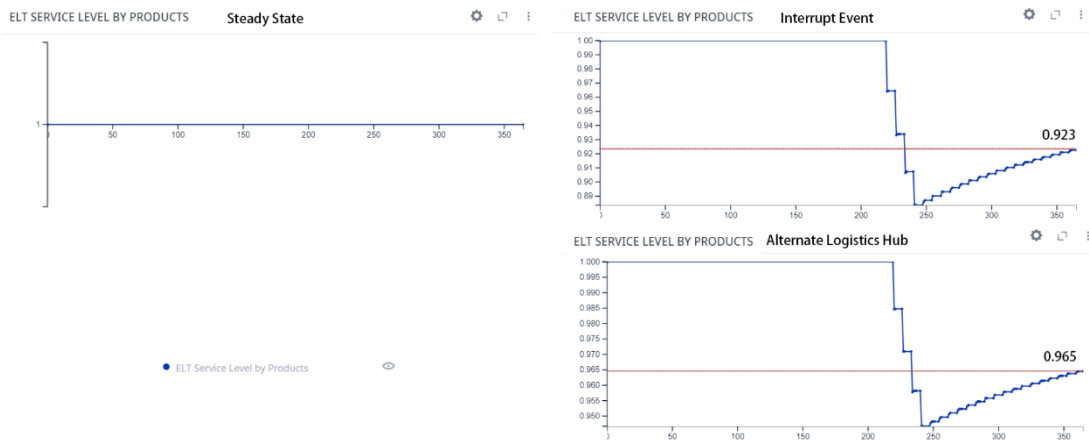


Figure 8. Service Level Comparison Across Simulation Scenarios

In addition, the new strategy helped the available inventory to form a cycle of inventory changes again and remain stable. Although the available inventory could not return to the normal fluctuation level within one month of the disruption after using the new strategy, a new fluctuation cycle was formed, indicating that the new strategy effectively mitigated the impact of the disruption event on inventory management, thus reducing the indirect impact of the ripple effect on the inventory level (e.g., Fig. 9). The new strategy effectively mitigates the demand disruption problem as can be clearly observed in Figure 10, where the number of orders received and processed is still proportional to time after the earthquake, indicating that the supply chain is still operating and has the capacity to process orders. Finally, the new strategy for product demand quantity is also effective in reducing the

number of delayed orders from 3600 to 1900 delayed orders, restoring the timeliness of order delivery and thus reducing the ripple effect (e.g., Figure 11). In summary and in conjunction with the research in the literature review, the twinning technique first simulated the supply chain after a disruption event and predicted the impact of the ripple effect on the aspirin supply chain. Then the digital technology used the network optimization technique to actively select the optimal response strategy. Comparing and analyzing the results of the three experiments, it can be concluded that the new strategy effectively reduces the impact of ripple effects on the supply chain, thus proving that the digital twin technology can effectively reduce the ripple effects in the pharmaceutical supply chain.

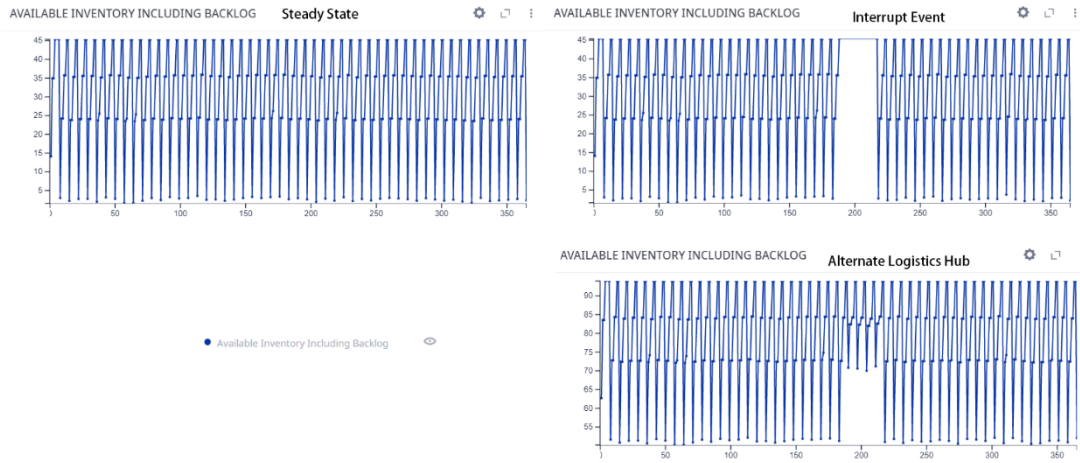


Figure 9. Inventory Stability Comparison Across Simulation Scenarios

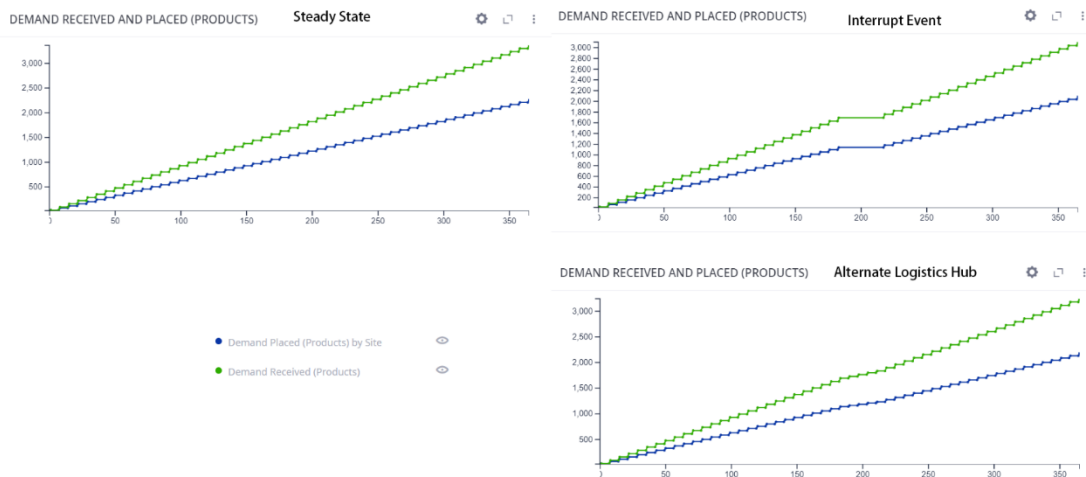


Figure 10. Impact of Disruption and Recovery Strategy on Demand Fulfillment



Figure 11. Effect of Recovery Strategy on Order Fulfillment and Delay Reduction

5.2. Validating Digital Twin Technology to Improve Supply Chain Agility

Since agility when connecting the digital twin technology and the ripple effect is key, in the process of analyzing the impact of digital twin technology on supply chain agility, the results of three experiments of sudden disruption events will be used for the demonstration. First, in terms of supply chain responsiveness, the higher the fulfillment rate of orders, the

more responsive the supply chain is. By comparing the results of the three simulations, it can be found (Figure 12) that the orders completed under normal circumstances and the customer's demand orders are almost synchronized, which indicates that the supply chain's responsiveness is very strong at this time, and the orders completed in the case where the logistics center is closed are obviously lagging behind the customer's demand orders, which indicates that a large number of orders can't be completed in time, and the supply

chain's responsiveness is insufficient. However, when the alternate logistics center is activated, although the completed orders still lag behind the customer's demand orders, the

degree of lag is significantly reduced, indicating that the new strategy improves the responsiveness of the supply chain.



Figure 12. Impact of Disruption and Recovery Strategy on Supply Chain Responsiveness

For the speed of the supply chain (Figure 13), the improvement of the digital twin technology on the speed of the supply chain is demonstrated by comparing the delivery time of three simulated supply chains. The supply chain that operates under normal conditions can respond to the customer's demand and complete the delivery of the order as fast as possible, and the supply chain under the disruption event has the longest delivery time and is higher than that of the delivery event after the emergency logistics center is activated, which shows that the strategy of setting up the emergency logistics center effectively improves the speed and responsiveness of the supply chain.

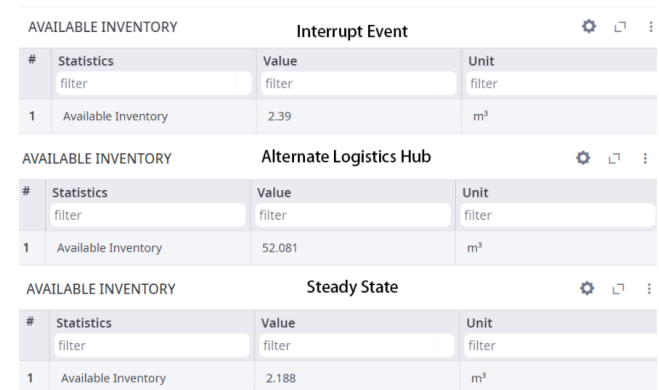


Figure 14. Impact of Digital Twin Strategy on Available Inventory for Supply Chain Proactivity

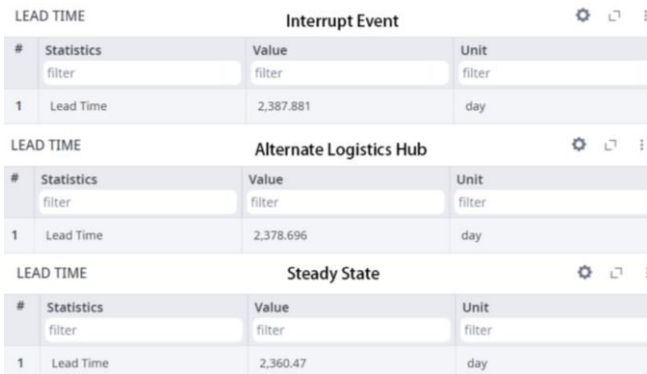


Figure 13. Comparison of Lead Times Across Supply Chain Scenarios

For supply chain proactivity, the impact of the digital twin technology on supply chain proactivity is assessed by comparing the available inventory of three supply chains (e.g., Figure 14). The supply chain using the new strategy has the most available inventory, indicating that the strategy provides additional inventory resources when disruptive events occur, enhancing supply chain proactivity, thus demonstrating that the digital twin technology improves supply chain proactivity.

Combining the results of the three simulation experiments, the supply chain after a disruption event quickly recovers from the seismic event through the new strategy, which illustrates the effectiveness of the new strategy, and proves that the digital technology improves the agility of the supply chain from the side of the digital technology. To summarize, the new strategy improves the supply chain's responsiveness, speed, proactivity, and flexibility, which proves that the digital twin technology improves the supply chain's agility.

The experimental results described above demonstrate the effectiveness of digital twin technology in improving supply chain agility and reducing the ripple effect. Specifically, the digital twin technology first simulates the supply chain and disruptions in the supply chain, then predicts the impact of the disruptions on the supply chain, and finally provides effective strategies to reduce the ripple effect. The experimental results from the three simulations validate two hypotheses; first, the simulated supply chain based on digital twin technology significantly improves the responsiveness, proactivity, flexibility, and speed of the supply chain, allowing the supply chain to demonstrate higher agility in the face of unexpected events. Second, the digital twin technology significantly reduces the ripple effect of the supply chain, which is manifested in five representative KPIs. Finally, 300 iterations

of the experiment ensure the stability and credibility of the results.

6. Conclusion

In this study, a pharmaceutical supply chain simulation model based on digital twin technology is constructed, through which the effectiveness of digital twin technology in improving supply chain agility and coping with ripple effects is verified. The experimental results show that digital twin technology significantly enhances the responsiveness, flexibility, speed and proactivity of the supply chain, which leads to higher agility and reduces the negative impacts of ripple effects in the face of sudden disruptions. This study not only illustrates the importance of digital twin technology in pharmaceutical supply chain, but also provides new ideas for pharmaceutical supply chain risk management. However, the study also has certain limitations that can be more comprehensively demonstrated and extended in the future.

First, the sensitivity analysis and t-test were not used for credibility analysis in analyzing the experimental results. Sensitivity analysis identifies key variables and parameters in the model, thus avoiding the influence of irrelevant factors on the experimental results. T-tests provide statistical significance verification to ensure that the experimental results are robust and authoritative. The lack of secondary validation may lead to a lack of reliability and accuracy in the results of the study, making the conclusions unconvincing. Second, this study failed to exclude the effects of other interfering factors on this experiment in advance. For example, there may be an interaction between the bullwhip effect and the ripple effect because there is an inverse function between the bullwhip effect and the ripple effect. If a sudden disruptive event occurs, it may lead to the simultaneous occurrence of the two effects, and it is impossible to distinguish the independent effects of the two effects. Finally, the models and cases used in this study are based on the 75mg aspirin supply chain in the London area and may not reflect the real situation of pharmaceutical supply chains in other countries and regions.

Despite the limitations of this experiment, the use of quantitative and qualitative methods comprehensively validates the great potential of digital twin technology in pharmaceutical supply chains, especially in improving supply chain agility and reducing the ripple effect. As digital technology continues to advance, digital twins can protect patients' lives and health more comprehensively in the future. First, digital twin technology can be combined with artificial neural network technology to build a more intelligent supply chain risk management system. Artificial neural network technology can utilize a large amount of historical data for training and self-learning to predict future demand changes and risk events in the supply chain, and the technology also improves the autonomy and responsiveness of the supply chain, which can further explore the impact of machine learning on the agility of the pharmaceutical supply chain. In addition, as pharmaceutical supply chain networks become more complex and diverse due to rapid globalization, the digital twin technology can be explored in the future to cope with transnational demand fluctuations and disruption events. Finally, digital twin technology can be utilized not only in the pharmaceutical supply chain, but also in the pharmaceutical industry, where digital twin technology can not only simulate the whole process of pharmaceuticals, but also optimize the production process and improve the quality of drugs.

Acknowledgements

Natural Science Foundation.

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APPENDIX

A1

#	Name filter	Type filter	Location filter	Initially Open filter	Inclusion Type filter	Capacity filter	Capacity Unit filter	Aggregate Orders by I filter	
1	Pfizer UK	Factory	Pfizer UK	<input checked="" type="checkbox"/>	Include	10,000	ton	<input type="checkbox"/>	
2	GSK	Factory	gsk	<input checked="" type="checkbox"/>	Include	10,000	ton	<input type="checkbox"/>	
3	Pfizer DC	DC	Pfizer DC	<input checked="" type="checkbox"/>	Include	0	m ³	<input type="checkbox"/>	
#	Customer filter	Product filter	Demand Type filter	Parameters	Time Period filter	Revenue filter	Currency filter	Expected Lead Time filter	Time Unit filter
1	Boots online shop	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
2	Cloud Pharmacy	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
3	Chemist Direct	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
4	Express Chemist	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
5	Superdrug online st	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
6	Boots	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
7	Lloyds Pharmacy	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
8	Superdrug	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
9	Well Pharmacy	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
10	Day Lewis Pharmac	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
11	St Thomas' Hospital	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
12	The Royal London H	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
13	Great Ormond Stree	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
14	The Royal Marsden	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
15	Hammersmith Hosp	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
16	Charing Cross Hosp	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
17	St Mary's Hospital	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
18	University College H	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
19	Moorfields Eye Hos	Aspirin	Periodic demand	Order interval: 7, Qu...	(All periods)	0	GBP	2	day
20	Guy's Hospital	Aspirin	Periodic demand	Order interval: 5, Qu...	(All periods)	0	GBP	30	day
#	Facility filter	Expense Type filter	Value filter	Currency filter	Time Unit filter	Product Unit filter	Time Period filter		
1	[Factory]	Other costs	30	USD	day		(All periods)		
2	Pfizer UK	Other costs	40	USD	day		(All periods)		
3	GSK	Other costs	40	USD	day		(All periods)		
4	[Factory]	Carrying cost	2	USD	day	m ³	(All periods)		
5	Pfizer UK	Carrying cost	7	USD	day	m ³	(All periods)		
6	GSK	Carrying cost	7	USD	day	m ³	(All periods)		
7	[Factory]	Facility cost	3	USD	day	m ³	(All periods)		
8	Pfizer UK	Facility cost	8	USD	day	m ³	(All periods)		
9	GSK	Facility cost	8	USD	day	m ³	(All periods)		