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Vaccine supply chain management: An intelligent system utilizing blockchain, IoT and machine learning

Hui Hu [a,b], Jiajun Xu [b], Mengqi Liu [c,*], Ming K. Lim [d]

[a] Economic Development Research Centre, Wuhan University, China
[b] School of Economics and Management, Wuhan University, China
[c] Business School, Hunan University, China
[d] Adam Smith Business School, University of Glasgow, UK

A R T I C L E I N F O

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A B S T R A C T

Vaccination offers health, economic, and social benefits. However, three major issues—vaccine quality, demand forecasting, and trust among stakeholders—persist in the vaccine supply chain (VSC), leading to inefficiencies. The COVID-19 pandemic has exacerbated weaknesses in the VSC, while presenting opportunities to apply digital technologies to manage it. For the first time, this study establishes an intelligent VSC management system that provides decision support for VSC management during the COVID-19 pandemic. The system combines blockchain, internet of things (IoT), and machine learning that effectively address the three issues in the VSC. The transparency of blockchain ensures trust among stakeholders. The real-time monitoring of vaccine status by the IoT ensures vaccine quality. Machine learning predicts vaccine demand and conducts sentiment analysis on vaccine reviews to help companies improve vaccine quality. The present study also reveals the implications for the management of supply chains, businesses, and government.

1. Introduction

Vaccination is the most economical and effective public health intervention to control infectious diseases (Adida et al., 2013). It also contributes to ending poverty and reducing inequality and is an essential means of achieving the United Nations Sustainable Development Goals (Decouttere et al., 2021). However, global vaccination coverage remains low due to inefficiencies in the vaccine supply chain (VSC) (Chandra & Kumar, 2018; Zaffran et al., 2013). Successful immunization programs are based on sustainable VSCs and logistics systems (Chandra & Kumar, 2018). One main objective of immunization programs is to optimize the VSC so that vaccines can be delivered safely and efficiently to the recipients. The VSC encompasses personnel, systems, equipment, and activities at all stages, including production, transportation, allocation, and distribution (Duijzer et al., 2018). At each node and along each channel, potential risks affect the efficiency of the entire VSC (Finkenstadt & Handfield, 2021). In sum, three key issues that need to be addressed are vaccine quality, demand forecasting, and trust among stakeholders (De Boeck et al., 2020; Duijzer et al., 2018).

Vaccine quality refers to various aspects, such as authenticity, safety, potency, and activity (Preiss et al., 2016). Counterfeit, defective, expired, and substandard vaccines are widespread around the world. Large number of counterfeit vaccine incidents, documented by the International Institute of Research Against Counterfeit Medicines, occurred primarily in Africa and Asia (Jarrett et al., 2020) (see Table 1). These counterfeit vaccines threaten public health and there is an urgent need for a credible anti-counterfeiting and traceability system to ensure the authenticity and safety of vaccines. Moreover, vaccines are usually temperature-sensitive and must be controlled within a certain range to maintain their potency and activity (Lin et al., 2020). However, vaccines are often exposed to inappropriate temperatures during transport (Hanson et al., 2017). Intelligent cold chain management is vital to ensure vaccine quality (Kartoglu & Milstien, 2014).

High uncertainty of supply and demand is a characteristic of the VSC (Duijzer et al., 2018). When the information flow is transmitted from the client to the supplier, it cannot be shared effectively. This magnifies the

Abbreviations: **BILSTM**, Bidirectional Long-Short Term Memory; **CNN**, Convolutional Neural Network; **dApp**, Decentralized Application; **DTs**, Digital Technologies; **GRU**, Gate Recurrent Unit; **IoT**, Internet of Things; **IPFS**, Interplanetary File System; **LSTM**, Long-Short Term Memory; **RFID**, Radio Frequency Identification; **RNN**, Recurrent Neural Network; **VSC**, Vaccine Supply Chain.

* Corresponding author.
E-mail address: liumengqi76@163.com (M. Liu).

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Table 1
Recorded events of counterfeit vaccines.

Year	Vaccine	Country/region where counterfeit vaccines were identified
2020	COVID-19	Russia
2020	COVID-19	Ecuador
2019	Rabies	Philippines
2019	Human papillomavirus (HPV)	Hong Kong
2019	Meningitis	Cameroon
2019	Cholera	Bangladesh
2019	Meningitis	Niger
2018	Chickenpox	Venezuela
2018	Hepatitis B	Uganda
2017	Diphtheria-tetanus-pertussis (DTP) triple vaccine	China
2017	Meningitis	Nigeria
2016	Rabies and meningitis	China
2016	Polio and hepatitis B	Indonesia
2016	Yellow fever	Angola

Source: Jarrett et al. (2020).

Table 2
Text classification accuracy of four deep learning models.

Rating	Static-CNN	Trainable-CNN	Static-BILSTM	Trainable-BILSTM	Support
1	0.7378	0.7437	0.7828	**0.7878**	7299
2	0.4386	0.5972	0.569	**0.6239**	2334
3	0.4236	0.5828	0.5403	**0.6058**	2205
4	0.3926	0.5769	0.5065	**0.6001**	1659
5	0.4341	0.5814	0.5442	**0.5953**	2710
6	0.3644	0.5621	0.4943	**0.5798**	2119
7	0.4107	0.5691	0.5178	**0.5851**	3091
8	0.4719	0.5795	0.5644	**0.5951**	6156
9	0.5394	0.613	0.6108	**0.6362**	9177
10	0.7565	0.7668	**0.7898**	0.7895	17,016
Macro avg.	0.4969	0.6173	0.592	0.6399	53,766
Weighted avg.	0.594	0.6664	0.6643	**0.6905**	53,766

information distortion and results in increasing fluctuations in demand information. This phenomenon is prevalent and is known as the "bullwhip effect" (Remko, 2020). Vaccine demand forecasts are based on target populations, estimated periods, and historical vaccination records. Nevertheless, the lack of reliable vaccination data and analysis methods results in the inappropriate analysis of vaccine utilization trends and inaccurate demand forecasts (Kaufmann et al., 2011). Production and procurement strategies based on inaccurate demand lead to loss of profits and additional costs (Chick et al., 2017).

Trust issues among stakeholders are prevalent in the health- and safety-related supply chains (Betcheva et al., 2021; Hobbs, 2020). In the VSC, conflicting goals and fragmented decision making among suppliers, organizations, and customers lead to a lack of trust among actors (Duijzer et al., 2018). Vaccine falsifications further deepen customers' distrust of suppliers (Jarrett et al., 2020). The public's lack of knowledge about immunization in some developing countries leads to distrust of immunization programs (Bangura et al., 2020) and decreases global immunization coverage (Weintraub et al., 2021). The long-lasting COVID-19 pandemic has exacerbated the weaknesses of the global supply chain (Edwards et al., 2021). The lockdowns caused by COVID-19 have limited supply chain processes (Guan et al., 2020; Karmaker et al., 2021). COVID-19 has disrupted routine immunization programs, impeded vaccines shipments, and increased demand uncertainty (Bloom et al., 2021). However, COVID-19 offers opportunities for VSC's sustainable development. On the one hand, growing public concern about health highlights the importance of vaccination (Dai and Song, 2021). On the other hand, digital technologies (DTs) have a greater appreciation for addressing supply chain management issues (Sarkis, 2020).

DTs have been used in the health care ecosystem for over a decade (Secundo et al., 2021). But their market penetration is slight due to strict regulation and poor supporting payment structures (Keesara et al., 2020). The COVID-19 pandemic offers a wide range of applications for DTs. Blockchain, the internet of things (IoT), artificial intelligence, machine learning, big data analysis, geospatial technology, and virtual and augmented reality have been widely used for COVID-19 detection, monitoring, diagnosing, screening, surveillance, and tracking (Chamola et al., 2020; Lee & Trimi, 2021; Mbunge et al., 2021). Digital transformation of the health care supply chain has become inevitable (Kraus et al., 2021).

In VSC management, the transparency, traceability, and immutability of blockchain can address vaccine safety issues and improve trust and coordination among stakeholders (Adarsh et al., 2021; Badhotiya et al., 2021; Cui et al., 2021; Liu et al., 2021). The literature discusses the use of the IoT in vaccine temperature detection (Monteleone et al., 2017), the application of artificial intelligence in vaccine development (Arora et al., 2021), and the operational value of using drones to transport vaccines (Haidari et al., 2016). These studies explore the potential application of DTs in the VSC, but they focus on the application scenario of a DT in a specific supply chain link (Liu et al., 2021). They neglect the management and operation of the VSC as a whole and the necessity for innovative integration among DTs. For example, while blockchain provides a platform for vaccine traceability and real-time vaccine consumption data, IoT sensors are still needed to monitor vaccine temperatures to ensure vaccine potency and data accuracy (Hasan et al., 2019; Singh et al., 2020). Machine learning is needed for data mining and analysis to generate practical applications (Ivanov & Dolgui, 2021).

This study aims to build an intelligent VSC management system from a holistic view, combining blockchain, IoT, and machine learning. The system efficiently manages the VSC affected by the COVID-19 pandemic and prioritizes three key issues: vaccine quality, demand forecasting, and stakeholder trust. This is an original work, as there is no integrated VSC management system with multiple DTs in the literature. Especially in the context of the COVID-19 pandemic, our designed intelligent VSC management system is a valuable contribution because it balances the intelligent management of both the short-term VSC and long-term immunization programs.

This work has important application implications, as it provides effective digital solutions to practical problems in the VSC. First, the combination of blockchain and the IoT addresses issues of vaccine quality and stakeholder trust and provides vast amounts of authentic real-time data. Second, using the Gated Recurrent Unit (GRU) machine learning model to forecast vaccine demand enables the average annual prediction error of influenza vaccine to stay within 3 %. Third, the trainable bidirectional long short-term memory (BILSTM) deep learning model provides sentiment analysis of vaccine reviews with nearly 80 % accuracy, providing strong support for enterprise credibility evaluation and consumer decision making. Finally, our proposed intelligent VSC management system is scalable and can enlighten other supply chains in terms of supply and demand management, security, and supervision.

The rest of this study is arranged as follows. Section 2 discusses the impact of the COVID-19 pandemic on the VSC and DTs applications. Section 3 presents the characteristics of blockchain, the IoT, and machine learning and their applications. Section 4 builds an intelligent VSC management system based on these three DTs. Section 5 analyzes data from blockchain platforms using machine learning. The study concludes with Section 6.

2. Impact of the COVID-19 pandemic on the health care and vaccine supply chains

This section discusses the risks posed by the COVID-19 pandemic to the health care supply chain and VSC, as well as the application of DTs.

2.1. COVID-19 pandemic risks to the health care and vaccine supply chains

Supply chain risks can be divided into operational and disruption risks (Fahimnia et al., 2018; Xu et al., 2020). Operational risk is mainly related to common disturbances in supply chain operation, such as demand fluctuations and early delivery times. Disruption risk mainly refers to events with low frequency and high impact (Kinra et al., 2020; Sreedevi & Saranga, 2017). The COVID-19 pandemic is a special case of supply chain disruption risk due to its long duration, high uncertainty, and chain reaction spread (El Baz & Ruel, 2021; Ivanov, 2020). The illnesses, deaths, and trade and travel restrictions caused by the COVID-19 pandemic have led to disruptions in supply chain networks (Nagurney, 2021).

The efficacy of a vaccine depends on its availability to the public. This means that the supply chain supporting vaccine production, transportation, allocation, and distribution must be resilient to quickly resume operations and continue to provide vaccines to the public after a disruption (Golan et al., 2021). Therefore, the problems in the VSC affected by COVID-19 must be properly addressed. The protracted COVID-19 pandemic has overtaxed health systems, with significant resources being devoted to responding to the surge of COVID-19 patients, thereby disrupting other preventive vaccination campaigns (Bloom et al., 2021; Zeitouny et al., 2021). The COVID-19 pandemic and associated disruptions resulted in 22.7 million children missing vaccinations, an increase of 3.7 million from 2019. In addition, movement restrictions to prevent COVID-19 infection have impeded international shipments of vaccines and exacerbated uncertainties in vaccine supply and demand. Moreover, as the COVID-19 vaccines continue to be developed, the risk of vaccine counterfeiting has become acute (Jarrett et al., 2020).

Although COVID-19 vaccine research has focused on developing the vaccine and measuring its effectiveness (Georgiadis & Georgiadis, 2021), the most critical response to the outbreak is not the vaccine itself, but vaccination (Dai & Song, 2021). Therefore, no link in the COVID-19 VSC can be ignored. Alam et al. (2021) identify 15 challenges in the COVID-19 VSC, among which the most critical challenges are the limited number of vaccine manufacturing companies, lack of vaccine monitoring institutions, difficulty in monitoring and controlling vaccine temperature, difficulty in organizing and coordinating vaccine distribution, and the high cost of vaccination. The supply chain of the COVID-19 vaccine, as a specific species of vaccine, also faces the same three key issues that we summarized in the introduction section: vaccine quality, uncertainty of vaccine supply and demand, and coordination among stakeholders.

2.2. COVID-19 pandemic brings opportunities for digital technology applications

Four themes recur in research related to the COVID-19 pandemic: the impact of the pandemic, supply chain resilience, supply chain sustainability, and DTs (Chowdhury et al., 2021; Sharma et al., 2020). Digitization has been the key deliverable from COVID-19 (Nandi et al., 2021). On the one hand, public health activities in response to the COVID-19 pandemic—such as mass population surveillance and screening, case identification, contact tracing, and evaluation of interventions based on mobility data and communication with the public—have facilitated the widespread adoption of DTs (Budd et al., 2020; Whitelaw et al., 2020). On the other hand, the lockdown and isolation measures in response to the COVID-19 pandemic forced people to keep their distance, pushing many behaviors (e.g., shopping, learning, working, meeting, and entertainment) to move from offline to online. New technology services have emerged to meet the needs of customers and businesses shopping and operating in the digital environment (Dwivedi et al., 2020; Pandey & Pal, 2020). All-round and multi-field digital transformation became inevitable (Kraus et al., 2021).

Vargo et al. (2021) summarize the use of DTs during the COVID-19 pandemic in four dimensions: technology, population, activity, and impact. They find that 28 different forms of technology, ranging from computers to artificial intelligence, have been used by eight groups of users, primarily health care professionals. Of these, 32 activities are involved, including remote delivery of health services, analysis of data, and communication. Among the many DTs, some key disruptive technologies are highlighted, including artificial intelligence, the IoT, big data, and blockchain (Abdel-Basset et al., 2021). These technologies provide digital transformation and research and development opportunities that not only help mitigate the negative impacts of COVID-19 but also help manage supply chains affected by COVID-19 (Chamola et al., 2020).

The role of DTs in responding to the COVID-19 pandemic has been extensively studied, but research related to the long-term digital management of the health care supply chain is insufficient. The application potential of blockchain technology in the health care supply chain has been explored to some extent. Ng et al. (2021) summarize the health care applications of blockchain, including artificial intelligence model development, medical supply chain encryption, and mobile health care, among others. Further, studies have shown that blockchain technology can be used in the VSC to address issues such as vaccine quality and safety, pricing and coordination, distribution and delivery, and improved trust among stakeholders (Adarsh et al., 2021; Antal et al., 2021; Badhotiya et al., 2021; Cui et al., 2021; Liu et al., 2021; Musamih et al., 2021; Yong et al., 2020). Yet, the potential of other DTs in the health care supply chain and VSC has not been explored in depth.

Ting et al. (2020) propose that DTs are highly interconnected, especially among the IoT, big data analysis, artificial intelligence, and blockchain. Specifically, the proliferation of IoT devices and instruments in hospitals enables the collection of real-time data at scale, which can then be used by artificial intelligence and deep learning systems to understand health care trends, model risk associations, and predict outcomes. Blockchain technology guarantees the security and traceability of the data used for modeling and prediction. Therefore, there is a need to integrate multiple DTs jointly to solve supply chain management problems. Since blockchain is a fundamental platform for integrating multiple DTs (Ng et al., 2021), it is feasible to construct an intelligent VSC management system based on blockchain technology and complemented by other DTs.

3. Digital technologies in supply chains

Traditional supply chains face many challenges, such as uncertainty, high costs, complexity, and vulnerability. To overcome these issues, supply chains must become more intelligent (Abdel-Basset et al., 2018). The COVID-19 pandemic further diminished supply chain efficiency, making it more urgent for organizations to implement data-driven technologies as part of their supply chain strategies. DTs have a significant impact on the nature and structure of supply chains, enabling internal integration of processes and, more importantly, external integration with suppliers and customers. This is achieved through improved communication and acquisition and transmission of data to enable effective decision making and improve supply chain performance. DTs have been an essential driver of effective supply chain management (Ross et al., 2010). They are vital in helping supply chains respond to changing environments and risks at all levels. In the following, we specify several important DTs and their application in supply chains.

3.1. Blockchain: Improving the security, visibility, and resilience of supply chains

Blockchain is a cryptographically secure distributed ledger that has the advantages of decentralization, information immutability, and transparency. The purpose of using blockchain is to solve the problem of

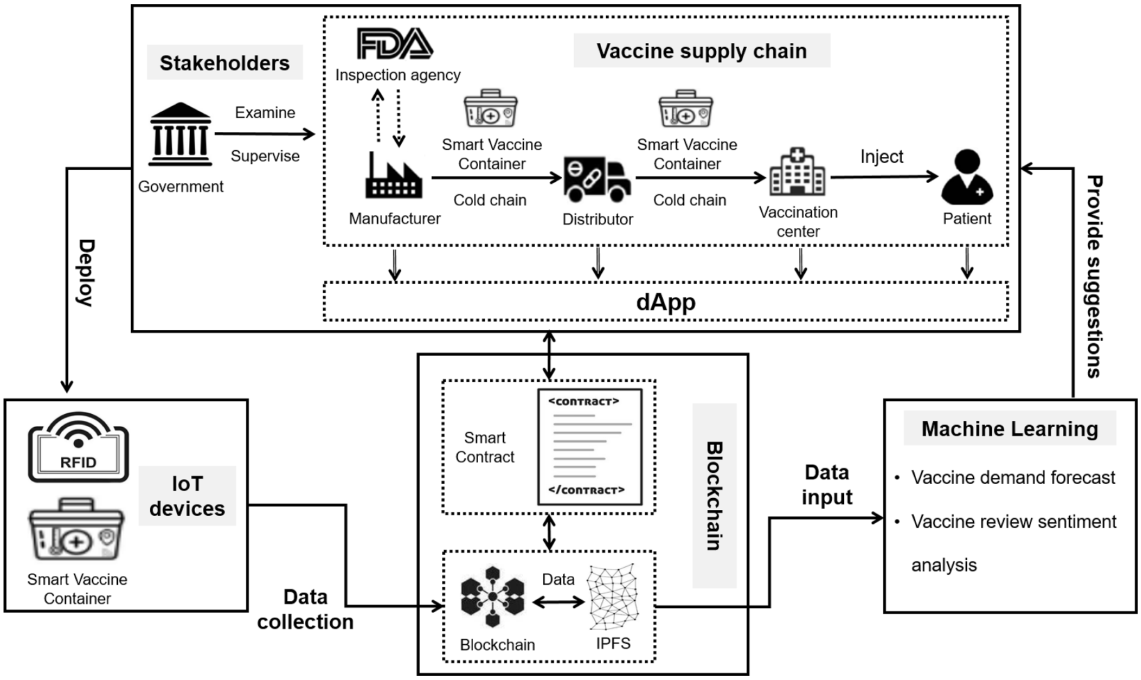

Fig. 1. The framework of an intelligent vaccine supply chain management system based on digital technologies.

overreliance on third parties in electronic payments. During the COVID-19 pandemic, many blockchain-related studies have highlighted its benefits for the supply chain management. First, the decentralized nature of blockchain increases supply chain resilience by mitigating the risks associated with intermediary intervention (Min, 2019). The reduced costs of labor, operation, and maintenance reduce the cost of supply chain transactions and improve management effectiveness (Catalini & Gans, 2020; Cole et al., 2019). Second, the immutable blockchain information combined with smart contracts can be used to coordinate supply chain members and enhance trust among stakeholders (Casado-Vara et al., 2018; Saberi et al., 2019). Third, the transparency of blockchain enhances the visibility of the supply chain, thus strengthening product security (Abeyratne & Monfared, 2016; Francisco & Swanson, 2018; Korpela et al., 2017).

In the wake of the COVID-19 outbreak, a large body of literature has emerged on the use of blockchain to solve health care supply chain problems. Marbouh et al. (2020) develop a blockchain-based tracking system for COVID-19 data collected from a variety of external sources. Yaqoob et al. (2021) apply blockchain to data management in health care. Omar et al. (2021) use blockchain smart contracts to automate procurement contracts in health care supply chains.

In the field of VSC, blockchain has been explored for every link. Alkhoori et al. (2021) introduce a blockchain-based smart container system (CryptoCargo) for safe and efficient distribution of vaccines. Adarsh et al. (2021) propose a traceable VSC (Immunochain) based on blockchain technology for immunization programs in India. Liu et al. (2021) analyze the pricing and coordination of the VSC based on blockchain technology and find that the introduction of blockchain technology increased the total profit, consumer surplus, and social welfare of the VSC. Musamih et al. (2021) propose an Ethereum blockchain-based solution for managing data related to COVID-19 vaccine distribution and delivery.

Moreover, blockchain applications in supply chains often work together with other cutting-edge technologies (Wamba & Queiroz, 2020). For example, blockchain can be combined with the IoT (De Villiers et al., 2021; Rejeb et al., 2019), big data analytics, and machine learning (Dwivedi et al., 2021).

3.2. Internet of things: Real-time monitoring and remote operation management

The IoT is an intuitive and scalable technology that conveys all relevant information in real-time across the supply chain via the internet (Manavalan and Jayakrishna, 2019). With the complexity of the network and more and more stakeholders, the end-to-end visibility of the supply chain becomes more critical (Pundir et al., 2019). However, technology adoption is still slower than current needs, and many supply chains still rely on manual processes for data recording, collection, and access. This approach is both complex and lagging and fails to handle the large-scale data effectively from the COVID-19 pandemic or identify and resolve supply chain issues promptly.

Applying IoT technologies to collect data and turn it into useful information provides visibility to supply chain participants. A typical example is the use of Radio Frequency Identification (RFID) technology to achieve fine-grained product tracking and tracing while reducing implementation costs (Li et al., 2017; Ustundag & Tanyas, 2009). Moreover, the IoT significantly reduces data acquisition time and enables the supply chain to respond to changes in real-time, thus increasing the efficiency of decision making (Ellis et al., 2015). For example, temperature-sensitive products can be monitored by IoT sensors to prevent product spoilage or expiration (Tajima, 2007). While saving labor costs, IoT technologies enable supply chain stakeholders to monitor the condition of products in real-time for timely decisions and coordination (Accorsi et al., 2017; Umair et al., 2021).

The combination of the IoT and other DTs is expected to enhance the role of the IoT. Research has concluded that the combination of machine learning technology and the IoT is promising because IoT devices automatically generate large amounts of data, providing a good basis for machine learning. In addition, the data provided by the IoT is safe and reliable. Combined with blockchain, it further promotes automation and solves the problem of blockchain data source forgery (Zelbst et al., 2019). Conversely, blockchain manages the accuracy of IoT devices and avoids malicious behavior through authentication (Chen et al., 2020; Wang et al., 2018); and the decentralized nature of blockchain is used to enhance the privacy and security of IoT systems (Banerjee et al., 2018; Kouzinopoulos et al., 2018).

3.3. Machine learning: Making decisions for supply chain uncertainties

Machine learning automatically improves computer algorithms through data or previous experience and provides more accurate decision results than humans in many areas (Ni et al., 2020). Making decisions based on uncertainty is an important problem in supply chains (Steckel et al., 2004), and machine learning solves this problem to some extent. Machine learning has performed well in production (Chen et al., 2012), demand prediction (Carbonneau et al., 2008), transportation and distribution optimization (Ćirović et al., 2014), inventory management improvement (Gumus et al., 2010), and supply chain risk prediction (Baryannis et al., 2019).

In recent years, several studies have explored the application of machine learning in the health care supply chain. Chatterjee et al. (2021) explore customer satisfaction in e-commerce for health care products, using text mining and machine learning techniques. Piccialli et al. (2021) predict medical appointments using machine learning models and hybrid neural networks.

The application of machine learning in supply chain management is still in the development stage (Ni et al., 2020), and its potential value needs to be further developed. However, using machine learning methods usually requires a large amount of data, and it is a significant challenge to collect the data efficiently and ensure its authenticity. Some studies suggest that this problem can be overcome by combining machine learning with other DTs, such as blockchain (Section 3.1) and the IoT (Section 3.2).

4. Intelligent vaccine supply chain management system

4.1. Overview of the system

This study designs a blockchain-based intelligent VSC management system combined with the IoT and machine learning (Fig. 1), which can track the whole vaccination process from manufacturers to end-users and provide decision support for VSC management. Trusted participants are vetted by the government to be eligible to join the system. Participants connect to the blockchain through a decentralized application (dApp). For vaccines to be delivered and traded in the supply chain, participants need to use this dApp to upload information about vaccines and transactions. The participants initiate vaccine transfer in the system, and the system verifies the data for compliance with the criteria through predefined smart contracts. After successful verification, the participants' records and transaction information are packaged and loaded into the system.

Among them, the blockchain mainly stores simple information and signatures of these transactions, while detailed vaccine information is stored in the InterPlanetary File System (IPFS). The decentralized and immutable nature of blockchain and IPFS ensures the authenticity of transaction records in the VSC. The IoT devices deployed during the transportation process monitor and track the vaccines and collect real-time monitoring data into the blockchain. In case of vaccine failures, such as expiration or high temperature, all relevant participants can obtain information on the abnormal status of the vaccine through the system. If there is a quality problem after a vaccine injection, accountability can be traced through the blockchain system to find the party responsible for the problem quickly. In addition, the large amount of reliable and real-time data on the blockchain can be used by research institutions or government agencies, for example, for big data analysis, combined with machine learning techniques to contribute to the improvement of supply chain management performance. More details of the system are provided in the following subsections.

4.2. Participants in the system

The key participants in the VSC include manufacturers, quality inspection agencies, distributors, vaccination centers, and patients. The government is included in the intelligent VSC management system. Participants must apply for an account (both public and private keys) with the government before they can join the vaccine supply chain, which the government releases only if the participant meets the required conditions. Vital records for vaccines with private key signatures also need to be uploaded when participants engage in transactions. The signatures are verified by the blockchain system to ensure that the records are correctly submitted by the respective institutions. These records are key to ensuring the quality of vaccines at every point in the supply chain. Among them, manufacturers provide vaccine production information; quality inspection agencies provide vaccine inspection reports; logistics companies provide real-time monitoring data on temperature, light level, and transport routes during vaccine transportation; and vaccination centers provide vaccination time and doctor information. The information provided may be falsified, so the government must regularly check the uploaded records. If there are any problems with the records, the corresponding agencies will be investigated and held accountable. Records and violations stored on and off the chain are accessible to all participants, promoting trust among participants in the VSC.

4.3. Basic technology of the system: Blockchain and smart contracts

Smart contracts are one of the appealing features of blockchain technology. They are a set of commitments defined in digital form to provide a transparent, free channel for all parties, allowing trusted, traceable, and irreversible transactions without third parties. Smart contracts are run exactly as programmed, without any possibility of downtime, fraud, or third-party interference. They are automatically triggered when the specified conditions are the same as the database events. Typically, smart contracts are stored in the distributed ledger of the blockchain platform and are fully protected from deletion and tampering. By designing the right smart contracts, our system intelligently monitors the state of the system and provides secure data.

Here we describe some of the key smart contracts in the system. First and foremost, once a participant initiates a vaccine transfer request, the system reviews the data submitted for compliance with the criteria through the predefined smart contracts. For vaccine manufacturers to transfer vaccines to logistics companies, the records must meet good manufacturing practices before the transfer is allowed. For the transfer of vaccines from logistics companies to vaccination centers, the records must meet the conditions of vaccine validity. If the vaccines have expired or failed in transit, by presetting smart contracts, information about vaccine failure will be disseminated throughout the VSC, preventing people from receiving ineffective vaccines. In addition, predefined smart contracts enable the system to provide intelligent oversight of the VSC. In the vaccine accident, blockchain will be used to track the entire process of vaccine circulation to investigate and pursue accountability.

Smart contracts can also be used to gather additional data for big data analysis by scientific institutions. For example, smart contracts incentivize users to provide vaccine reviews by giving them coins on the blockchain, and then text sentiment analysis using machine learning technology evaluates the credibility of enterprises. Alternatively, a marketplace for buying and selling personal vaccination data can be formed through smart contracts, where vaccination users choose to sell their age, medical history, and other data. Machine learning technology can analyze the data to enable vaccine development and personalized vaccination recommendations. Thus, combining smart contracts and machine learning provides big data analysis and makes management recommendations for the VSC.

4.4. Assurance technologies for the system: IoT and IPFS

Blockchain databases are trusted in untrusted environments (Tsolakis et al., 2021). The uploaded data in blockchain have the advantage of

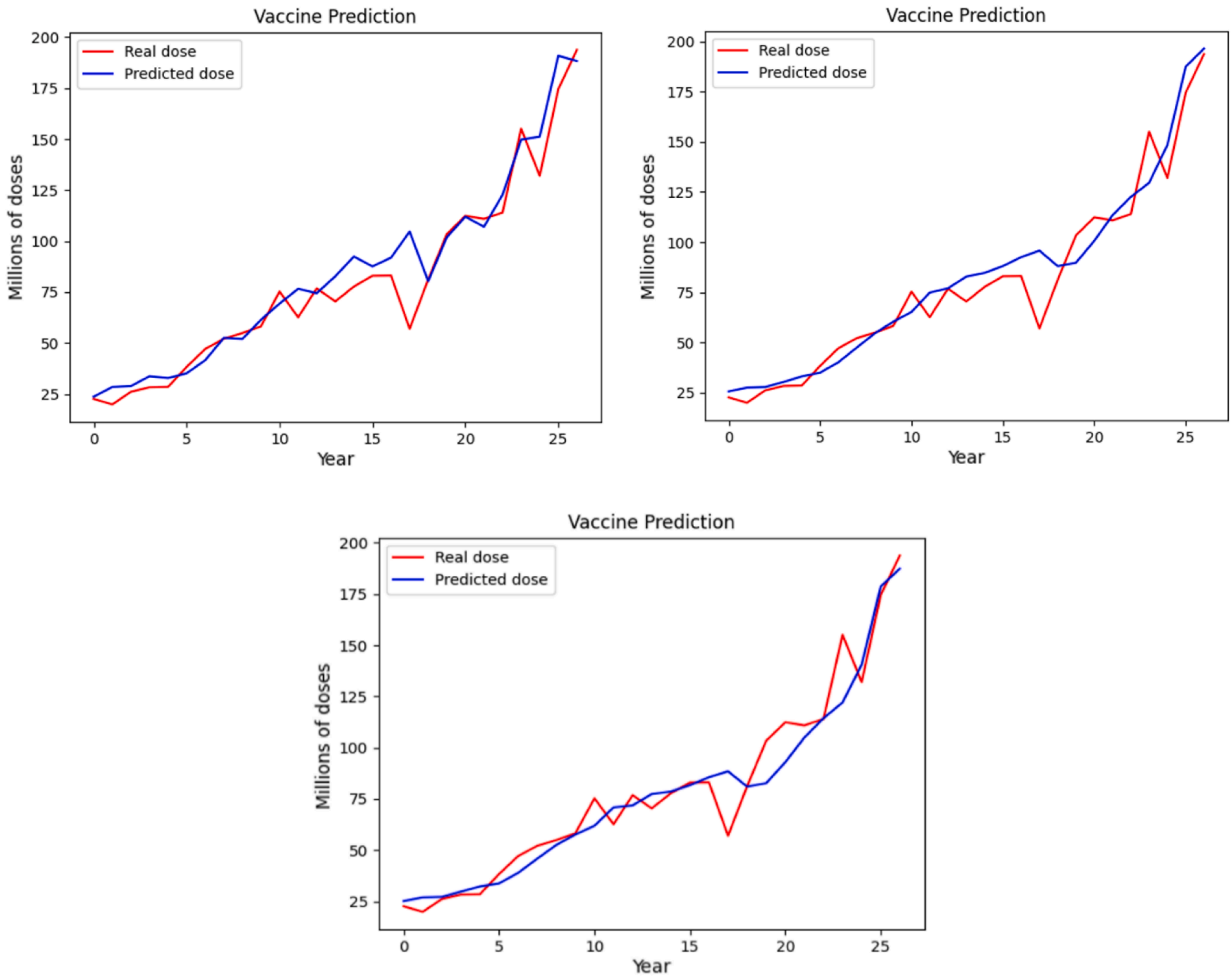

Fig. 2. Vaccine demand forecasting based on three machine learning models.

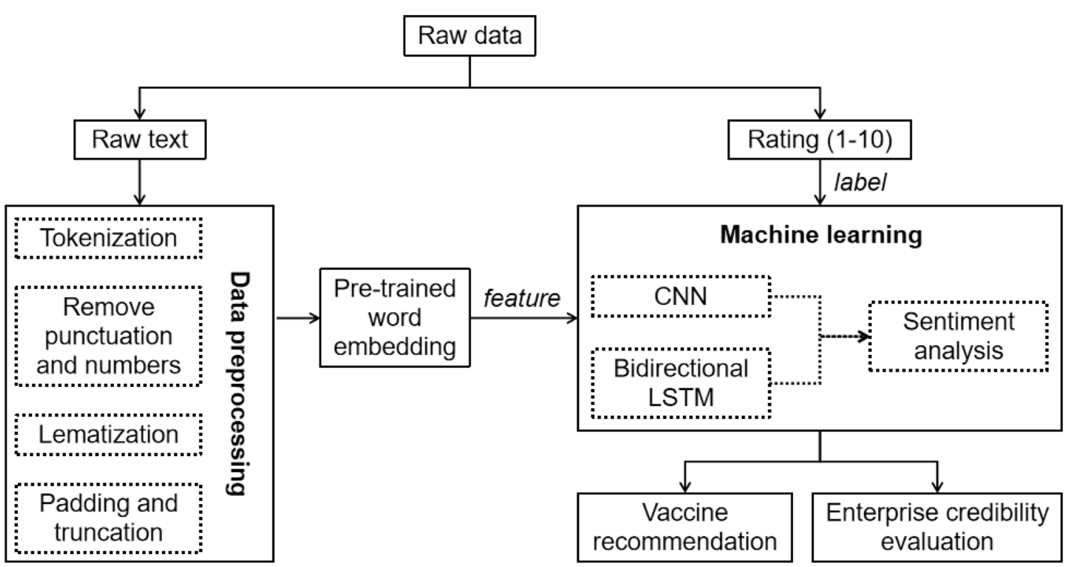

Fig. 3. Process for sentiment analysis of vaccine reviews.

being untamable, but it is difficult to solve the problem of forgery in data collection. Automation of the IoT ensures data accuracy as it eliminates human errors and intentional fraud, which lead to wrong information. In addition, the volume of data in the blockchain is growing due to the feature of not being able to delete but only to add. Blockchain needs to be supported by new storage technologies to achieve scaling. Therefore, the DTs supporting the blockchain-based intelligent VSC management system designed in this study also include the IoT and IPFS.

4.4.1. Internet of things: Efficient access to real information

Our system combines the advantages of the IoT and blockchain: the former solves the problem of how to get real information efficiently and the latter solves the problem of trust with its immutability and information transparency.

RFID is a non-contact data communication technology that automatically identifies tags and input information (Angeles, 2005). RFID technology has a high identification accuracy even in harsh working environments (Mondal et al., 2019). Our system assigns a unique RFID tag to each vaccine as it is packaged by the manufacturer to reduce the labor cost of entering vaccine information. It also prevents human error in data collection and ensures the authenticity and accuracy of the data on the chain, while the blockchain further ensures that there can be no tampering with the data on the chain. The combination of blockchain and RFID provides full vaccine traceability and greatly enhances vaccine safety.

In addition, IoT sensing devices are used to monitor the status of vaccines during transportation (Hasan et al., 2019). Vaccines are thermosensitive and photosensitive, and there is a risk of vaccine expiration or failure during transport, which has been exacerbated during the COVID-19 pandemic (Alam et al., 2021). Real-time monitoring of vaccine temperature during transport can prevent vaccine failure. The vaccines are placed in smart containers with IoT sensors, which automatically digitize the real-time monitored temperature and light status and send violation information to the blockchain system through smart contracts. The intelligent VSC management system greatly improves the transparency of the supply chain and enhances the credibility of information through the combination of the IoT and blockchain technology, enabling the identification and tracking of information throughout the VSC.

4.4.2. InterPlanetary File System: Avoiding blockchain information explosion

IoT sensors provide real-time and continuous monitoring data for the blockchain, but the accompanying huge data storage and the increasing number of participants on the blockchain may lead to an information explosion (Wang et al., 2021). Our system uses the IPFS to solve this problem. The IPFS is a decentralized storage network with fast file storage and downloading, and the distributed storage feature ensures that the data inside are not arbitrarily tampered with or deleted (Zheng et al., 2018). A block in a traditional blockchain consists of a header and a body. The header is mainly used to verify the correctness of transactions and stores a smaller volume of data. The body stores specific transaction data and other larger data, which occupy most of the space in the blockchain. Our system keeps the body in IPFS, a design that greatly reduces the size of the blockchain and thus avoids blockchain information explosion.

4.5. Decision support technology for the system: Machine learning

Blockchain and IoT enable access to real information, while the use of machine learning models allows analysis of the data and provision of useful recommendations to participants based on the results. Reliability and sharing of data are important in machine learning to improve the accuracy of the results. Blockchain motivates and collects real data and machine learning processes the data to make accurate decisions. The combination of the two provides highly accurate results (Tanwar et al., 2019). The intelligent VSC management system of this study combines blockchain and machine learning to form a system in which the two constantly promote each other. In the next section, we specify how machine learning techniques are used in this intelligent system to provide decision support for participants and thus improve the management performance of the VSC.

5. Decision support analysis of the intelligent vaccine supply chain management system

In this section, we use machine learning to analyze two intelligent VSC management systems' cases—vaccine demand forecasting and vaccine review sentiment analysis. Thereby, machine learning provides decision support to solve two important issues of VSC (vaccine demand forecasting and vaccine quality management). It is worth noting that the data used in the two cases are not collected by the proposed intelligent VSC management system. However, we discuss the advantages of the data collected by the proposed system compared to traditional data.

5.1. Vaccine demand forecasting

The imbalance between vaccine supply and demand is a prominent issue in the VSC, especially in the context of the COVID-19 pandemic. Incorrect estimation of vaccine demand is also a major cause of vaccine expiration. Supply exceeding demand results in wasteful use of resources, while greater demand than supply leads to vaccine nationalism and the risk of price fraud (Eccleston-Turner & Upton, 2021; Nhamo et al., 2021). Therefore, accurate forecasting of vaccine demand is critical for vaccine production. In our system, vaccination centers provide real-time vaccine usage quantity data to the blockchain, which is vaccine demand data. Using machine learning to train the data and time-series models to predict demand and contribute to less vaccine expiration. Among the many machine learning models, RNN, LSTM, and GRU models are often used. In the following, we compare the performance of the three models for vaccine demand forecasting with a specific data set.

We use the U.S. influenza vaccination volume (million doses) from 1980 to 2020 as the vaccine demand forecasting dataset, with the data from 1980 to 2011 as the training set and the data from 2012 to 2020 as the testing set. We designed RNN, LSTM and GRU models to predict the demand for influenza vaccines, respectively. The vaccination doses predict the vaccine demand for each year from the previous seven years. The trends of predicted and actual amounts for the three models are shown in Fig. 2.

In the figure, all three models, especially the GRU model, have almost identical trends in predicted and actual doses of the influenza vaccine. There is no overfitting between the predicted and actual amounts, suggesting that the prediction models are scalable. Further, we compare the errors of the three machine learning models calculated using different metrics (see Appendix Table A.1). The results show that GRU is more accurate than LSTM and RNN in vaccine demand prediction. If the GRU model is applied to predict the demand for influenza vaccine and keep the annual remaining vaccine ratio within about 3 % of the predicted value, a balance between vaccine supply and demand will be effectively achieved. According to Rappuoli et al. (2019), the global vaccine market will reach $62 billion by 2027, and the COVID-19 pandemic will increase this value significantly. Therefore, using appropriate machine learning models to predict vaccine demand will help the health care sector and vaccine enterprises save billions of dollars annually.

Due to data limitations, the case study only provides annual vaccine demand forecasts for the United States. The proposed intelligent system will provide timely and accurate vaccine demand data down to the city and even hospital level. A fine-grained vaccine demand forecast would offer a critical reference for vaccine distribution within a country. The blockchain and IoT in the proposed system make the data more credible, which will further improve the demand forecasting accuracy.

5.2. Sentiment analysis of vaccine reviews

Providing safe and effective vaccines to consumers has always been an essential concern for VSC management, and consumer satisfaction is the most direct response to vaccine quality. The literature has conducted consumer satisfaction surveys but has rarely examined online reviews

(Chatterjee et al., 2021). Sentiment analysis using machine learning is good at understanding the attitudes of online reviews (Bag et al., 2019; Fan et al., 2017). In our proposed system, reviews from vaccine consumers can first be collected using the incentives of the blockchain. The vaccine reviews in the blockchain could then be mined and analyzed using a text sentiment analysis model to help vaccine companies better understand consumer attitudes and needs. On the one hand, this supports the system in recommending to consumers high-quality vaccines that meet individual needs. On the other hand, it promotes vaccine enterprises to compete to improve vaccine quality and address consumers' concerns. Fig. 3 illustrates the process of vaccine review sentiment analysis.

We use the data set proposed by Grasser et al. (2018) as a case study, which is a collection of 215,063 online drug reviews obtained from the Drugs.com website. Table A.2 in the Appendix shows vaccine-related examples of scores 1 to 10 in the data set, where reviews and ratings are used as features and labels for the machine learning model. To validate the generalizability of the machine learning model on the new data set, we divide the corpus into a training set and a testing set, at a ratio of 75:25. Fig. A.1 in the Appendix shows the ratings distribution in the training and testing sets. The distribution has a polarized character, where the number of reviews with ratings of 1, 8, 9, and 10 accounts for 74 % of the overall sample, indicating that consumers' reviews are significantly emotional. Before inputting them into the machine learning model, we preprocess the data, which includes tokenization, removing punctuation and numbers, lemmatization, padding, and truncation. Then, we compare the Convolutional Neural Network (CNN) and BILSTM models to find a suitable model and show the results of the two models for the trainable and static data sets.

F1-score is the most commonly used metric to measure the accuracy of text classification. Table 2 shows the F1-scores of the four models for each classification, where *support* represents the number of samples per class and *rating* represents the score. The *macro average* is a simple average of the F1-scores for each classification, and the *weighted average* is the average obtained by assigning the sample size of each class as the weight.

As can be seen, the accuracy of the four models differed little in identifying reviews with apparent emotions. However, they show significant differences in identifying reviews with intermediate attitudes, where the trainable-BILSTM model has higher accuracy than the other models for almost all classifications (except for the rating of 10). This proves that the trainable-BILSTM model is the most suitable deep learning model for sentiment analysis of vaccine reviews.

The number of consumer reviews is essential for improving the efficiency and accuracy of the model (Hwang et al., 2020). One of the advantages of the proposed system is encouraging consumers' comments with the help of blockchain tokens payment system (Yong et al., 2020). Using the proposed system to collect vaccine reviews, we can continue training based on the trained model to improve the accuracy of text sentiment analysis. Consumers' attitudes toward vaccines, including side effects and utility after vaccination, will be captured automatically. This will provide an essential reference for consumers and manufacturers to help vaccine quality continue to improve.

6. Discussion and conclusion

To manage the COVID-19-affected VSC, we combined blockchain, the IoT, and machine learning to build an intelligent VSC management system. The research has important implications for both theory and practice.

6.1. Theoretical implications

In the context of the continuing spread of COVID-19, relevant studies have focused on managing the COVID-19 VSC. This particular attention is reasonable but has led to a lack of research on the supply chain management of the many routine vaccines affected by COVID-19. We bridge this gap, as the intelligent VSC management system is applicable not only to COVID-19 VSC management but also to routine VSC management affected by COVID-19.

Meanwhile, this study highlights the critical role of the combined application of DTs in solving the pressing problems faced by VSC. The respective benefits of blockchain, IoT, and machine learning applications in the supply chain are relatively well established in the literature. However, these DTs are usually applied separately in supply chain systems. In the proposed system, we further combine the three DTs by complementing each other to provide more significant benefits in the VSC than they could individually. IoT ensures efficient and accurate blockchain data collection. Machine learning relies on extensive and trusted amounts of data from the IoT and blockchain as input. In turn, the suggestions derived from machine learning contribute to the reliable operation of the supply chain and the ongoing generation of useful data records. Our study indicates that the combined application of these three DTs provides significant joint benefits to the VSC. Our proposed Intelligent VSC management system contributes to the existing literature by helping to better understand how different DTs can be combined in general supply chain management. Also, it expands the use and fields of application of DTs and contributes to the advancement of research in supply chain management.

6.2. Practical implications

6.2.1. Implications for supply chain management

There are three critical issues in the VSC: vaccine quality, demand forecasting, and trust among stakeholders. The recent outbreak of the COVID-19 pandemic has made these three issues even more challenging. Our proposed intelligent VSC management system solves these three major problems to a large extent.

In terms of *vaccine quality*, blockchain's decentralization and data immutability effectively avoid vaccine counterfeiting and ensure the authenticity and safety of vaccines. The IoT-based smart containers enable real-time monitoring of all vaccine information during the circulation process, ensuring the potency and activity of the vaccines. These merits help to cope with the national and international disruption of vaccine shipments brought about by the COVID-19 pandemic. Further, text sentiment classification models in machine learning enable accurate interpretation of the vaccine review data stored in the blockchain platform, facilitating all vaccine enterprises to improve vaccine quality and address consumers' concerns. In particular, the trainable BILSTM model provides a high accuracy rate of nearly 80 %. The continued training based on the pre-trained model in the future can continuously improve the accuracy of text sentiment analysis to help to enhance the quality of the vaccine.

As for *demand forecasting*, the open and transparent data in blockchain make the transmission of information real and reliable, avoiding the risk of the "bullwhip effect". Moreover, based on the data stored in the blockchain, the time-series machine learning prediction models allow for a more accurate prediction of vaccine demand. For example, when using the GRU model to predict the demand for influenza vaccine in the United States, it is possible to keep the average annual prediction error within 3 %, which helps coordinate the supply and demand of the vaccine. Vaccine demand during the Covid-19 pandemic is highly uncertain, and accurate predictions by machine learning will provide considerable cost savings to the VSC.

On *trust issues among stakeholders*, blockchain and the IoT allow all relevant participants in the system to track the status of vaccine delivery in real-time and enable rapid traceability for accountability, greatly enhancing trust among participants. The system guarantees the safety and effectiveness of vaccines and encourages enterprises to improve the quality, which further enhances customers' trust in suppliers. This will improve supply chain resilience and enable VSC to recover quickly after the Covid-19 pandemic.

Thus, our research has practical significance, as it effectively solves actual problems in the VSC, especially during the COVID-19 pandemic. In addition, the intelligent system we constructed is scalable. It is not only applicable to the VSC, but also provides management insights for other supply chains to solve problems of supply and demand, security, and supervision.

6.2.2. Implications for business management

While improving demand forecasting accuracy and motivating enterprises to enhance product quality, our system also highlights the importance of consumers' online reviews. Current customer satisfaction surveys are often conducted through questionnaires, ignoring the value of online reviews. Enterprises must be aware that consumers' online reviews are data that can and should be leveraged. Online reviews are massive and transparent. Consumers use them to learn about the information and quality of different enterprises' products to make their consumption decisions. Enterprises use them to understand customers' needs and other enterprises' products and achieve more competitive product improvements. Machine learning is a significant processing and analyzing tool for large-scale data, and collecting more data is essential to improve the accuracy of the analysis. Therefore, enterprises should adopt business strategies to motivate consumers to make online reviews.

6.2.3. Implications for government management

The credibility of the system requires the government to take on more responsibility. First, implementing the intelligent VSC management system requires the collaborative efforts of many participants and high costs. The government should lead, organize, and coordinate all parties and bear most of the investment. Second, although this blockchain-based system is transparent, some hidden frauds still need to be detected by the government. Therefore, at the beginning of the system's operation, it is the government's responsibility to vet the participants, and those who pass the vetting process are eligible to join the system. During the operation of the system, the government should check the records uploaded by each participant and disclose and hold them accountable for violations. This will enhance the trust among the participants in the supply chain. In addition, we highlighted another important trust issue: the lack of public knowledge about immunization leads to mistrust in the national immunization program, thus hindering immunization coverage. So popularizing immunization knowledge is an important task for the government. Similarly, the ethical and moral risks associated with the widespread use of DTs have caused concerns in the public mind that need to be alleviated through government-guided actions, which would contribute to the innovative development of DTs.

6.3. Limitations and future research

We used past vaccination doses for the vaccine demand forecast. However, population size, vaccine prices, immunization awareness, and local policies are all influencing factors (Chiu et al., 2008; Dizbay & Öztürkoğlu, 2020; Sarkar et al., 2020; Wong et al., 2020). Complex models considering various factors can be constructed in the future to predict vaccine demand more accurately. Our proposed intelligent VSC management system also has implementations and adaptation challenges. A major challenge is the costs of implementation, energy consumption, and operations. Despite the benefits of an efficient and smart VSC system, the considerable upfront cost in the integrated application of DTs may hinder the implementation of this system. The cost includes the installation and maintenance cost of the large number of IoT devices, the transaction cost of real-time blockchain monitoring, and the computational cost of fine-grained machine learning. Therefore, a valuable direction for research is to reduce the cost of applying multiple DTs.

Disclosure of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Hui Hu: Writing – original draft. **Jiajun Xu:** Software, Investigation. **Mengqi Liu:** Writing – review & editing, Project administration. **Ming K. Lim:** Supervision, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix

See the Tables A.1 and A.2.
See the Fig. A.1.

Table A.1
Computational errors of the three machine learning models.

	RNN	LSTM	GRU
Mean absolute error (million doses)	10.07	7.21	**5.42**
Root mean square error (million doses)	10.37	9.02	**5.97**
Mean absolute percentage error (%)	5.55	3.16	**3.02**

Table A.2
Vaccine-related examples of consumer reviews in the data set.

ID	Vaccine	Review	Rating
90,103	Pneumococcal 13-valent vaccine	I have suffered extreme muscle stiffness and weakness in my back, shoulders, and legs since taking this vaccine. I have also developed a chronic upper respiratory infection. This vaccine should be taken off the market.	1
214,931	Human papillomavirus vaccine	Given to daughter at age 13. Diagnosed with chronic idiopathic thrombocytopenic purpura at age 13.5 years. Side effects list bruising, bleeding tendency, and red pin picks on skin. Are the several side effects due to a temporary decrease in platelet function, much like aspirin or the trigger of a platelet antibody?	2

(*continued on next page*)

Table A.2 (*continued*)

ID	Vaccine	Review	Rating
180,871	Influenza virus vaccine, inactivated	There was no pain at the injection site. Both my boyfriend and I received the shot and had close to the same experience, except I have been having extreme vomiting, after 2 weeks of getting the shot. We both experienced a severe headache starting within 30 min of receiving the shot that lasted about a day and a half, followed by severe diarrhea that is still ongoing, three weeks from the time of injection with nausea. He is having lots of muscle aches still, while I'm having severe pain in one of my legs near the hip. Neither of us had problems or sickness before the shot that would indicate it was something other than the shot.	3
88,838	Mumps virus vaccine	Lots of itching all over the body, sometimes severe.	4
90,112	Pneumococcal 13-valent vaccine	Side effects of injection include very sore arm effectively rendered useless. Muscle aches and joint pain without relief would not allow me to sleep. Fatigue and back pain plus headache contributed to an overall miserable night and day. I do not know how long this will continue, it has been 36 h. This vaccine requires at least two days off work and should be accompanied by a good narcotic.	5
193,708	Influenza virus vaccine, live, trivalent	This was very simple to use. I thought it would be great. My 3-year-old has vomiting as a side effect. My 6-year-old and I seem to have no side effects.	6
230,081	Meningococcal group B vaccine	My child got a headache, fever for two days after having the Bexsero vaccine. It made me worry about if she will get meningitis disease.	7
214,942	Human papillomavirus vaccine	I got the shot, the second one hurt the most. The pain in my arm only lasted maybe 2 h at the most. When I got the last shot, the nurse injected it into the joint of my shoulder, which hurt for a lot longer but that was the nurse's fault, not the Gardasil. I had no side effects. I believe getting the vaccination was a smart thing to do and was worth it.	8
180,874	Influenza virus vaccine, inactivated	Barely felt the pinch. Just a little redness, bump around the injection and itchiness for a few days. Not sore at all compared to regular shots.	9
46,651	Gardasil vaccine	I am 18 years old and have had all three of these shots. I don't understand why people make this shot to be such a big deal. It barely hurt when I got them. Even if it did, who cares? If the shot is going to help you out in the long run. I never had any bad side effects. I recommend it to any woman who likes to be proactive.	10

Source: *Drugs.com* website.

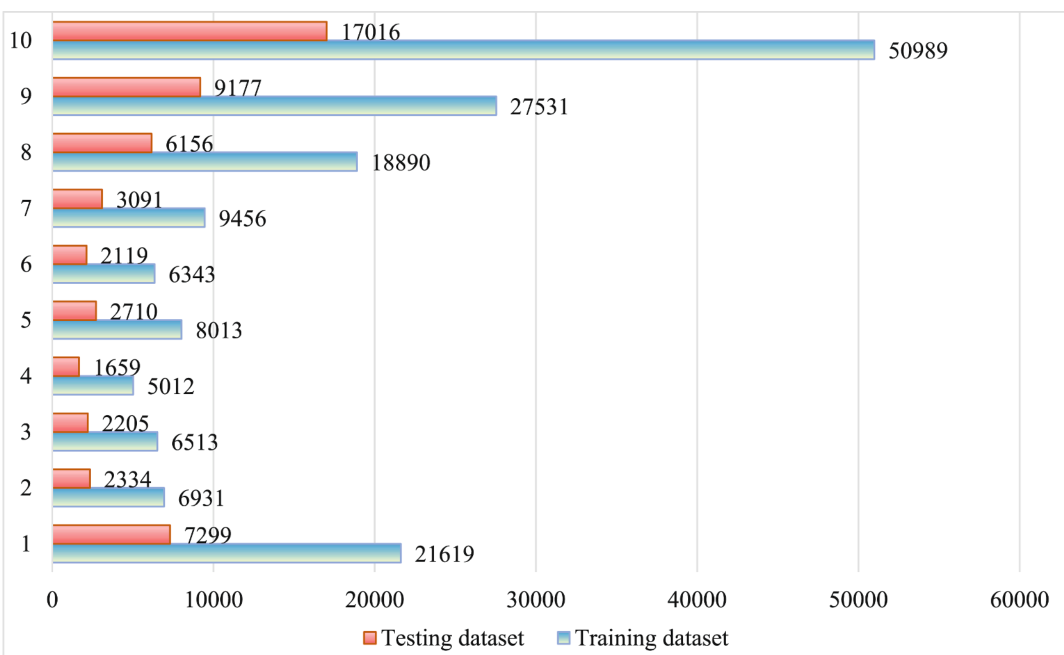

Fig. A.1. Rating distribution in the training and testing sets.

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Hui Hu is an Associate Professor in Business Economics and Management at Wuhan University. His research interests are in the area of sustainable production and consumption and sustainable supply chain. His work has been published in journals such as Emerging Markets Finance & Trade, Journal of Cleaner Production, Applied Energy, Energy, IET Renewable Power Generation, Journal of Intelligent and Fuzzy Systems and Australasian Accounting Business and Finance Journal.

Jiajun Xu is a Research Fellow and Ph.D. Student at Wuhan University. His research interests are in the area of business analytics and management.

Mengqi Liu is an Associate Professor in Operations Management at Hunan University. His research interests are in the area of supply chain and operational research. His work has been published in journals such as European Journal of Operational Research, International Journal of Production Research, Journal of Industrial & Management Optimization, International Transactions in Operational Research, Asia-Pacific Journal of Operational

Research, Annals of Operations Research, Transportation Research Part E-Logistics and Transportation Review and Omega.

Ming K. Lim is currently a Professor of Supply Chain Management and Digitalization at the Adam Smith Business School, University of Glasgow. Before joining the University of Glasgow, he was Dean of the College of Mechanical Engineering and Distinguished Professor of Manufacturing & Logistics Engineering at Chongqing University and Co-cluster Lead/Professor of Supply Chain and Operations Management at Coventry University. Professor Lim is Editor-in-Chief of the International Journal of Logistics Research and Applications and an editorial board member of a range of leading journals. He has published over 175 papers in leading journals in the fields, such as Int. J. of Operations & Production Management, European J. of Operational Research, Int. J. of Production Economics, Omega, Transportation Research, Computers & Industrial Engineering, J. of the Operational Research Society, Annals of Operations Research, Int. J. of Production Research, Production Planning and Control, Expert Systems with Applications, Resources, Conservation & Recycling, and Industrial Management & Data System.