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Urban monitoring, evaluation and application of COVID-19 listed vaccine effectiveness: a health code blockchain study

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ABSTRACT

Objective By using health code blockchain, cities can maximise the use of personal information while maximising the protection of personal privacy in the monitoring and evaluation of the effectiveness of listed vaccines.

Design This study constructs an urban COVID-19 listed vaccine effectiveness (VE) monitoring, evaluation and application system based on the health code blockchain. This study uses this system and statistical simulation to analyse three urban application scenarios, namely evaluating the vaccination rate (VR) and determining the optimal vaccination strategy, evaluating herd immunity and monitoring the VE on variant.

Main outcome measures The primary outcomes first establish an urban COVID-19 listed VE monitoring, evaluation and application system by using the health code blockchain, combined with the dynamic monitoring model of VE, the evaluation index system of VE and the monitoring and evaluation system of personal privacy information use, and then three measures are analysed in urban simulation: one is to take the index reflecting urban population mobility as the weight to calculate the comprehensive VR, the second is to calculate the comprehensive basic reproduction number (R) in the presence of asymptomatic persons, the third is to compare the difference between the observed effectiveness and the true effectiveness of listed vaccines under virus variation.

Results Combining this system and simulation, this study finds: (1) The comprehensive VR, which is weighted to reflect urban population mobility, is more accurate than the simple VR which does not take into account urban population mobility. Based on population mobility, the algorithm principle of urban optimal vaccination strategy is given. In the simulation of urban listed vaccination involving six regions, programmes 1 and 5 have the best protective effect among the eight vaccination programmes, and the optimal vaccination order is 3-5-2-4-6-1. (2) In the presence of asymptomatic conditions, the basic reproduction number, namely R0*(1-VR*VE), does not accurately reflect the effect of herd immunity, but the comprehensive basic reproduction number (R) should be used. The R is directly proportional to the proportion of asymptomatic people (aw) and the duration of the incubation period (ip), and inversely proportional to the VR, the VE and the number of days transmitted in the ip (k). In the simulation analysis, when symptomatic R0=3, even with aw=0.2, the R decreases to nearly 1 until the VR reaches 95%. When aw=0.8, even when the entire population is vaccinated, namely VR=1, the R is 1.688, and still significantly greater than 1. If the R is to be reduced to 1, the VE needs to be increased to 0.87. (3) This system can more comprehensively and accurately grasp the impact of the variant virus on urban VE. The traditional epidemiological investigation can lose the contacts of infected persons, which leads to the deviation between the observed effectiveness and the true effectiveness. Virus variation aggravates the loss, and then increases the deviation. Simulation case 1 assumes the unvaccinated rate of 0.8, the ongoing VR of 0.1, the completed VR of 0.1 and an average infection rate of 2% for the variant virus. If a vaccine is more than 90% effectiveness against the premutant virus, but only 80% effectiveness against the mutant virus, and because 80% of the unvaccinated people who are not infected are not observed, the observed effectiveness of the vaccine is 91.76%, it will lead to the wrong judgement that the VE against the variant virus is not decreased. Simulation case 2 assumes the unvaccinated rate of 0.8, the ongoing VR of 0.1, the completed VR of 0.1 and an average infection rate of 5% for the variant virus. Simulation finds that the higher the proportion of unvaccinated infected people who are not observed, the lower the estimate of observed effectiveness; and the lower the true effectiveness, the larger the gap between observed effectiveness and true

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study combines health code, blockchain and statistical methods to propose a new epidemiological investigation system.
⇒ Cities use the system to monitor and evaluate the effectiveness of listed vaccines.
⇒ The system does not consider the control of people and objects from outside the city that may carry the virus.
⇒ People in different stages of development and different cultural backgrounds have different sensitivity, scope and intensity of privacy protection, which is not discussed in the system.
⇒ The system does not take into account factors such as city size, blockchain shortcomings in security, latency, throughput, scalability, interactivity, etc.

effectiveness. Simulation case 3 assumes the unvaccinated rate of 0.2, the ongoing VR of 0.2, the completed VR of 0.6 and an average infection rate of 2% for the variant virus. Simulation finds that the higher the proportion of unobserved completed vaccination patients who are not infected, the lower the estimate of observed effectiveness; and the lower the true effectiveness, the larger the gap between observed effectiveness and true effectiveness. Simulation case 4 assumes the unvaccinated rate of 0.2, the ongoing VR of 0.2, the completed VR of 0.6 and an average infection rate of 5% for the variant virus. If a vaccine is more than 90% effectiveness against the premutant virus, but only 80% effectiveness against the mutant virus, and because 80% of the infected people with complete vaccination are not observed, the observed effectiveness of the vaccine is 91.95%, similar to case 1, it will lead to the wrong judgement that the VE against the variant virus is not decreased.

Conclusion Compared with traditional epidemiological investigation, this system can meet the challenges of accelerating virus variation and a large number of asymptomatic people, dynamically monitor and accurately evaluate the effectiveness of listed vaccines and maximise personal privacy without locking down the relevant area or city. This system established in this study could serve as a universal template for monitoring and evaluating the effectiveness of COVID-19 listed vaccines in cities around the world. If this system can be promoted globally, it will promote countries to strengthen unity and cooperation and enhance the global ability to respond to COVID-19.

INTRODUCTION

The COVID-19 outbreak continues to be a global pandemic. Vaccination, as the most advantageous weapon in curbing COVID-19,[1] plays an increasingly important role in fighting COVID-19.[2] Simulation studies show that high vaccination rates (VR) can effectively inhibit the spread of the virus.[3] The rising VRs in countries around the world effectively curb the spread of the epidemic and reduce the symptoms and mortality of infected people.

The effectiveness of listed vaccines has always been the focus of public attention. Traditional vaccine development takes about 10–12 years from preclinical development to approval, production and vaccination. More than 250 COVID-19 vaccines are currently being developed,[4] and over 90 vaccines are developed in the middle and late clinical research stages.[5] At present, there are three kinds and five brands of COVID-19 vaccines approved for listing with conditions in China: inactivated vaccines (produced by Beijing Institute of Biological Products and Wuhan Institute of Biological Products under China Biotechnology of China Pharmaceutical Group, and Sinovac Biotech), adenovirus vector vaccine (produced by CanSino Biologics) and recombinant COVID-19 vaccine (produced by Zhi Fei Long Ke Ma Biopharmaceutical).[6 7] Most of the approved COVID-19 vaccines are in emergency use or listed with conditions, and the data on the effectiveness of the vaccines are mainly derived from clinical trial results.[8–23] However, due to the limited number of clinical trial observation samples and the short trial period, these conclusions also lack a large enough sample and a long enough observation period for scientific demonstration. There is no sufficient evidence that any vaccine prevents 100% of COVID-19.[24 25] The effectiveness results of vaccines in clinical trials are commonality data, and clinical trials of vaccines and vaccine marketing are usually at different stages of epidemic development, most clinical trials are in the early stage and outbreak stage and most marketing is in the late stage of the outbreak. People need to know more about the reality (non-clinical trials) for their own (individual characteristics), as well as the varieties and combinations of vaccines suitable for them.[26 27]

Epidemiological investigation is the main method to monitor the effectiveness of listed vaccines (hereinafter referred to as vaccines) in the world (including in cities) at present.[28–31] The traditional epidemiological investigation adopts the method of ex post facto tracing. The rapid variability of COVID-19 and the large presence of asymptomatic people pose great challenges to the traditional epidemiological investigation of passive monitoring.

At present, with the rapid spread of COVID-19, the variation is also accelerating. Britain, South Africa, Brazil, India, Peru and other countries appeared in the variant strain of the virus transmission speed, infection intensity, and harm is greater than in the early stages of COVID-19. Take Guangzhou in May 2021 as an example, the Delta variant strain imported from abroad infected 47 cases in five generations in only 10 days.[32 33] The Centers for Disease Control and Prevention found the Delta variant strain R0 up to 8–9.[34] Although the vaccines now used are still valid for these variant strains,[35–39] the vaccines' effectiveness is weakening.[40–45] For example, the proportion of completed Delta deaths in the UK increased from 29% on 13 June 2021 to 42.7% on 25 June.[46] Another example, the data released by the Israeli Ministry of Health on 5 July 2021 showed that the effectiveness of Pfizer vaccine decreased by about 30%–64% in the prevention of symptomatic COVID-19 cases,[47] and the data of 22 July showed an efficiency reduction to 39%.[48] There are also studies showing that COVID-19 variant strains pose severe challenges to current vaccines.[49 50] WHO experts and British scientists do not rule out the failure of some or even all of the existing vaccines.[51 52] It is more urgent that people need to know the vaccine effectiveness (VE) against the variant virus and the way of additional vaccination.[53–62] Moreover, the enhancement of the variant virus transmission force is also changing the way of transmission. The incubation period is significantly shortened and the start time of transmission is earlier. In the past, it was mainly transmitted through close contact, but now it can be transmitted in the same space.[63 64] The concept of close contact personnel has changed significantly, and its number and scope are much larger than the original definition. This poses a great challenge to the traditional epidemiological investigation.

Because the traditional epidemiological investigation cannot be fully traced, it has been difficult to find patient zero and asymptomatic infections in COVID-19 prevention and control. If patient zero happens to be asymptomatic, it is more difficult and sometimes impossible to find the zero patient through the traditional epidemiological investigation. If patient zero and asymptomatic

carriers are not found or the number of asymptomatic carriers is not accurate enough. This will bring loopholes in COVID-19 prevention and control, and also affect the accurate assessment of the VE and herd immunity. In the accelerated variation of COVID-19, infected persons are more initially asymptomatic.[32] The vaccines reduce the symptoms of those infected, making asymptomatic people more common.[65] This situation is particularly prominent in the outbreak of Omicron strain.[66] All these bring new challenges to the traditional epidemiological investigation.

Health code is the first digital epidemic prevention measure launched in Hangzhou in China in the form of international QR code as the carrier, and quickly launched in more than 100 cities across the country, becoming an important tool for epidemic prevention all over China. At the end of February 2020, China's National Government Service Platform launched the 'Epidemic Prevention and Health Information Code' to promote the exchange and mutual recognition of the national 'health code'. After the health code, China set up a travel code, and the Ministry of Industry and Information Technology organised the China Institute of Information and Communications and three basic telecommunications companies to launch 'communication big data travel card' to collect personal location track information. The card mainly collects the cities that people have visited in 14 days. At present, the health code platform has combined the health code and the travel code, and has absorbed the health, industry and information technology, transportation, customs, immigration management, civil aviation, railway and other information. In China, city health code (platform) belongs to a centralised information management mode, to master a large number of personal privacy information. After China, South Korea, France and other countries have also launched personal information codes similar to the China health code. Some countries, such as the USA, use Bluetooth contact tracking tools to establish decentralised health code based on protecting personal privacy, but the effect is not ideal.[67]

At present, in some epidemic outbreak cities, in order to help epidemiological investigations meet these challenges and to effectively curb the epidemic, some have taken the very strict practice of locking down the whole epidemic-related area or even the whole city. Health code (platform) has been used to assist in epidemiological investigations in some Chinese cities, and multiple rounds of nucleic acid testing and screening are carried out for all.[68] The epidemiological investigation based on health code adopts the way of pretracking, which can be regarded as a new type of epidemiological investigation. In terms of practical effects, it can immediately block the spread of the epidemic in low-mobility areas,[69] conduct comprehensive screening of the infected and asymptomatic persons, and provide a comprehensive and accurate understanding of VE in the early stages of the outbreak, and make finding patient zero much easier. At the same time, due to the use of a large number of personal privacy information collected by the health code in this process, coupled with the opacity of the use of methods and content, some people worry that personal privacy protection is not getting due attention.[70] The lockdown has severely cracked down on economic development. How can health code be used to accurately monitor and evaluate the effectiveness of listed vaccines while maximising the protection of personal privacy, without locking down the relevant area or city?

As one of the most disruptive innovations in the new generation of information technology revolution, blockchain[71] has many excellent characteristics, such as decentralised and networked digital trust, network-wide consensus and value incentive maintenance, fairness and transparency, anonymity and tamper proof, traceability and smart contract, rights protection and inclusiveness. However, it is also facing legal, security, privacy, latency, throughput, scalability, interactivity, resource utilisation and many other issues and challenges. Blockchain has been widely used in digital finance, Internet of Things (IOT), intelligent manufacturing, supply chain management, government services, health and other fields since its launch in 2008. Some research focuses on its application of vaccine supply traceability.[72 73] After the outbreak of COVID-19, blockchain has played an important role in charitable donation, material transfer, community epidemic prevention, vaccine supply traceability and other aspects.[74–76]

At present, COVID-19 is still spreading around the world, the virus mutation is accelerating and the development of the epidemic is more uncertain. Countries like China with better epidemic control are facing huge pressure from the imported cases. At the same time, some countries with severe epidemics have improved significantly with the widespread use of vaccines, and their opening up has gradually resumed. They also face input pressure from the epidemic, especially from mutant strains and asymptomatic persons. Therefore, it is urgent to build a unified epidemic tracking and traceability information platform. To sum up the respective health code practices in China, Europe and the USA, in order to establish a widely accepted and unified model, humans must find an effective way to maximising the use of personal information and maximising the protection of personal privacy. A feasible practice is to combine health code and blockchain, and make use of the anonymity, traceability, tamper proof, smart contract and many other technical characteristics of blockchain, to combine centralised management and decentralised technology and to build a unified and effective global system for monitoring, evaluation, prevention and control of COVID-19.[77]

This study is to apply this idea to the urban monitoring and evaluation of the effectiveness of COVID-19 listed vaccines. Based on the health code blockchain platform, this study believes that a normalised all-around real-time system can be considered to actively monitor and evaluate the effectiveness of listed vaccines. This system combines centralised management with decentralised technology

to implement the principles of 'privacy information available but invisible', 'tolerating the lack of information', and incorporate individual vaccination information into the health code blockchain, and use blockchain technology to track, trace and monitor individual vaccination, health status (including vaccination response, vaccine effect), action trajectory, protection status, etc.

The use of the individual privacy information is based on the emergency degree of the antiepidemic state in the system. The antiepidemic state is usually divided into emergency, more emergency and non-emergency. The use of private (sensitive) information in personal records should be in three ways: non-anonymous (non-desensitised), semi-anonymous (semi-desensitised) and anonymous (desensitised). Three urban application scenarios of the monitoring, evaluation and application system are discussed later: evaluate the VR and determine the optimal vaccination strategy; evaluate herd immunity; and monitor the VE on variant virus. From the perspective of antiepidemic situation, the former scene corresponds to a non-emergency state, taking anonymous (desensitisation) for the use of privacy (sensitive) information in personal records; the latter two are emergency states, and taking not anonymous (not desensitisation) for the use of privacy (sensitive) information in personal records. In either state, even in an emergency, departments that use personal privacy information cannot access personal privacy information directly. This shows that the maximum protection of personal privacy in the fight against the epidemic is not absolute and unconditional, but relative and conditional.

The system can fully track the path of the virus transmission, and dynamically monitor and accurately evaluate the effectiveness of the vaccination and the fight against the variant virus, and trace the virus to find zero and asymptomatic patients. It is an active monitoring mode that integrates vaccine technology and digital technology to cover the whole people in the city, which can carry out all aspects, all processes and all-time and space monitoring and evaluation of the VE, and protect personal privacy to the maximum extent. This precise system does not need to lock down the relevant area or city, but only seals off the relevant elementary units according to needs by tracing the action trajectory and protection status of infected persons and their contacts.

METHODS

The urban COVID-19 VE monitoring, evaluation and application system established in this study includes four parts: the health code blockchain platform, the listed VE dynamic monitoring model, the VE evaluation index system and the monitoring and evaluation system of personal privacy information use.

Construction of a health code blockchain platform containing vaccination conditions

Health code and information of the health code holder

At present, the health code used all over China is one person, one code, generally divided into three colours: green, yellow and red. Green code means that the holder is healthy and can be free to move; yellow code means that the holder is physically unsound or surrounded by confirmed or suspected cases, and needs to be isolated for observation and nucleic acid test, and if there is nothing wrong, the code will be converted back to green; red code indicates that the holder is a confirmed or suspected case, and will be converted to green code after isolation or treatment for health. Wang and Zhao add blue and orange to health code.[77] The blue code is between green and yellow codes, indicating that the holder has abnormal body but is free to move through protection; the orange code indicates close contact with confirmed or suspected cases, which has been adopted in some places.

Some cities in China have begun to show the vaccination information with health code, such as Chongqing and Wuhan. The golden border of health code indicates the holder has completed vaccination, and needle patterns in four corners of health code indicate the number of shots. This method of marking vaccination information is not complete, usually only marking completed vaccination, not the vaccination that has started but has not been completed. In order to ensure the completeness of the vaccination information, the unfinished vaccination status needs to be marked. Guangdong province has noticed this using green squares in the middle of the health code to indicate the start of vaccination, and golden squares to indicate that vaccination has been completed. Germany is about to launch a mobile phone QR code as a digital certificate for COVID-19 vaccination and plans to launch it in the other European Union countries. Of course, there is a risk of exposing the privacy information of non-vaccinators by marking the vaccinator information on the health code, because some of them are not vaccinated not because of their subjective wishes but for objective reasons. Therefore, the marking method of vaccination should be based on personal wishes and adopt a variety of alternative methods. One way is to mark the health code directly through special pattern matching, and another way is to attach relevant vaccination supporting information outside the health code.

Based on the above and combined with the practice of using health code, this study represents the vaccinators in green, yellow, orange and red with a border pattern. See table 1 for various specific meanings.

The holder information attached to the health code is far richer and more valuable than the health code itself. The accompanying information proposed by Wang and Zhao includes four categories: the holder's basic personal information, health information, protection status information and action trajectory information.[77] In order to accurately understand the personal antiepidemic situation, this includes a large amount of personal privacy

Table 1 Health code colour definition in the health code blockchain

Health code colour	Meaning
Green	Without any infection, can go out normally.
Yellow	Abnormal health or confirmed patients nearby, need to be isolated and observed at home or go out after passing the nucleic acid test.
Orange	Having contact with confirmed patients (or cured after diagnosis) requires centralised isolation and observation.
Red	Confirmed patients, need to have centralised isolation treatment.
No borders	No vaccination.
Grid borders	Vaccinated or require additional vaccination.
Solid borders	Complete vaccination or complete additional vaccination.

information. In order to track and monitor the effectiveness of the vaccines, it is also necessary to increase the relevant information reflecting the owner's vaccination, including vaccine name, vaccination situation, adverse reactions, vaccination effect, etc.

Track the action trajectory of the health code holder

The action trajectory of the urban health code holder (hereinafter referred to as the holder) is usually determined by his or her occupation, life habits and social relations. The action trajectory is of strong regularity, that is, in addition to going out, vacation, medical treatment, visiting relatives, parties and other special circumstances, in most normal situations such as work and shopping, the action trajectory basically maintains a fixed mode in time and space. Even in some special cases, such as medical treatment and visiting relatives, there are certain action rules to follow. Therefore, the rules and basic patterns of the holder's action trajectory can be mined through the use of artificial intelligence and other methods with the help of big data analysis of the action historical trajectory of the holder. A basic feature of the system is the tolerance of holder information shortage: there may be a large lack of holder action trajectory information in practical operation. We can virtually fill the missing information of the holder action trajectory by mining the trajectory rules and basic patterns. Of course, the virtual filling is done through smart contracts. For the protection of the holder's privacy information, the virtual patching also follows the principle of 'available but invisible'. This mining analysis can also predict the future trajectory of the holder's action, and contribute to the relevant simulation research. To sum up, it greatly reduces the overall cost of tracking and improves tracking efficiency and accuracy.

Design of health code blockchain platform architecture

For a city, it can be constructed as an alliance chain based on role (node) hierarchical decentralisation (table 2). The basic features of this architecture are as follows.

First, build a complete vaccination-related information management system with relative division of labour and mutual restriction through the hierarchical decentralisation of roles. The municipal government has the right to build and manage the systems, and the district-level government and relevant departments have the right to establish vaccination information and the right to use it according to the status of the epidemic, and shall accept the supervision of the holders and the specialised supervisory organisation. The holder has various rights of personal information management and has the right to know, supervise and inquire about various users of personal information.

Second, build two types of blockchains to fully trace the vaccination-related information. One is the blockchain (hereinafter referred to as the record blockchain) that tracks the holder vaccination and records the complete information of individual vaccination, health and action trajectory through privacy information desensitisation (such as using dynamic anonymous identifiers for personal identity and action trajectory). In practice, a unified recording blockchain can be established, or multiple recording blockchains can be established according to different categories such as vaccination, health and action trajectory. You can even consider linking only the hash value of the recorded information. The complete information is stored on the personal phone by encryption, and the complete information is desensitised through privacy information and is stored on different public clouds hosted by corresponding government departments as backup according to different parts such as vaccination, health and action trajectory. Even if the information on the personal mobile phone is lost, the complete recorded information can be restored to the personal mobile phone by using the personal privacy information and its dynamic anonymous identifier comparison library established by the municipal government and combined with the above public cloud.

One is the blockchain that tracks the use of personal record information (hereinafter referred to as the use blockchain). Urban district-level governments and health departments use the vaccine monitoring data (including personal record information) with the prepared smart contracts according to the emergency situation and their antiepidemic responsibilities, and write their usage into the blockchain. However, the district-level governments and health departments cannot directly access personal privacy information, so as to truly make personal privacy information available and invisible in this process. When using personal record information, especially privacy (sensitive) information, district governments and health departments should write the usage details into the blockchain through desensitisation, and timely feedback to the

Table 2 List of roles, functions and data rights of the main institutions in the system

Main institutions (node)	The role	Function	Main rights for personal data, blockchain
Municipal government	System design, construction and maintenance	► Establish standard specifications for system operation and use. ► Lead the implementation of system networking and management networks. ► Establish various institutions and the corresponding subrole classification authority directory, and implement and supervise them, and punish illegal institutions. ► Develop personal privacy (sensitive) information encryption methods and personal identity dynamic anonymous identifier and use key database, spatial location dynamic anonymous identifier and use key database. Provide different dynamic anonymous identifier and use key databases about personal identity and spatial location for different units.	► Build and manage all kinds of dynamic anonymous identifier and use key database, backup public cloud systems, record blockchain and use blockchain systems, but cannot directly call (query) to the record blockchain and the use blockchain.
District-level government	System operation and use	► According to the role authorisation, use the personal identity dynamic anonymous identifier database and the spatial location dynamic anonymous identifier database provided by the municipal government, compare the personal record information by storing your personal mobile phone (health code) with the backup cloud and write to the blockchain through the personal identity information desensitisation. ► Monitor and manage the antiepidemic situation in the region according to the role authorisation. ► Use smart contracts to release information and requirements such as the epidemic and personal vaccination to the holder, and dynamically adjust the holder's personal health code. ► According to the role authorisation, in cooperation with health departments, use smart contracts to use record blockchain to carry out vaccine effectiveness monitoring and relevant scene application. ► Write the usage of the holder's personal records into the record blockchain.	► Establish two types of blocks (the record blockchain and the use blockchain). ► Use various personal data in the record blockchain based on two types of use key databases according to the antiepidemic emergency. ► Cannot directly access personal privacy information.
Health departments, medical (scientific research) institutions, etc	System operation and use	► Monitor the holder's health, vaccination status according to the role authorisation and combined with the health code, and feed it back to the holder's personal mobile phone (health code). ► Use personal identity dynamic anonymous identifier database provided by the municipal government to upload personal identifiable information after desensitisation of health and vaccination information to a separate public cloud for backup. ► According to the role authorisation, with the cooperation of district-level governments, carry out epidemic prevention and control, and use the smart contract and the record blockchain to carry out the vaccine effectiveness monitoring and the application of relevant scenarios. ► Write the usage of the holder's personal records into the record blockchain.	► Provide desensitisation personal health and vaccination record information. ► Use various personal data in the record blockchain based on two types of use key databases according to the antiepidemic emergency. ► Cannot directly access personal privacy information.
Transportation departments (communication departments, social institutions), etc	System operation	► Use health code and other methods to collect the action trajectory (protection status) of the holder based on the role authorisation, and feedback to the public's personal mobile phone (health code). ► Use the personal identity dynamic anonymous identifier and spatial location dynamic anonymous identifier database provided by the municipal government to upload the action trajectory and protection status of the holder's personal identity information and spatial location information after desensitisation to a separate public cloud for backup, and shall not retain the record information.	► Provide record information on personal action trajectory after desensitisation.

Continued

Table 2 Continued

Main institutions (node)	The role	Function	Main rights for personal data, blockchain
Internet (blockchain, big data) companies	System technical support and maintenance	► Provide and update various technical support required by the system to maintain its normal operation. ► Provide training for system users (holders).	
Person	System use and supervision	► Monitor own health status and action trajectory (protection status) using health code. ► Use mobile phone (health code) to receive personal health and action trajectory information collected by relevant departments and institutions, and to manage all kinds of encrypted personal information. ► Use smart contracts to know the epidemic dynamics and take corresponding epidemic prevention measures. ► Use smart contracts to master the use of personal record information, especially privacy (sensitive) information, and report relevant problems to the special supervisory organisation.	► Access personal data in various public clouds. ► Access the individual-related data in the record blockchain and the use blockchain. ► Can question the correction of the personal data in the public cloud and in the record blockchain, and request an amendment.
Specialised supervisory organisation	System supervision	► Supervise the whole system according to the role authorisation to ensure the safe operation of the system. ► Supervise the illegal authorisation of all institutions. ► Accept the holder's request to investigate the illegal use of personal information and report the findings to the municipal government.	► Supervise and question the illegal use of personal data, the record blockchain and the use blockchain.

holder himself, and accept the supervision of the holder himself and the specialised supervisory organisation.

Third, use smart contracts to carry out holder information management, use and scene application to ensure that the use of holder information is implemented in accordance with the predetermined way and content norms. The advantage of a smart contract is that its execution is transparent to all affiliates, cannot be modified privately and can be executed automatically. This advantage of smart contracts makes both the district-level governments and relevant departments automatically implement contracts according to the established holder information, and such automatic implementation is transparent and preaware of the information holder. The use of smart contracts can effectively dispel holder concerns about the misuse of holder information by government departments.

VE dynamic monitoring model

The urban VE dynamic monitoring model is conducted by using the health code blockchain to track and monitor the holder's health and vaccination status, action trajectory and protection status. The basic principle is shown in figure 1. In the process of virus traceability, centralised quarantine or home quarantine, in order to quickly find the infected person, multiple rounds of nucleic acid testing and screening can be carried out for all the people involved. Of course, the model can be used to monitor the safety of the listed vaccines.

VE evaluation index system and monitoring

Main evaluation indicators

Simple effectiveness and comprehensive effectiveness

In order to accurately grasp the effectiveness of the vaccines, urban vaccinators are divided into two categories: complete vaccination and in vaccination. Each category is quantified by the maximum severity of the symptoms present. Symptoms (sy) are defined as level 5: 0—uninfection, 1—infection asymptomatic, 2—infection mild, 3—infection severe, 4—death. $sy_i^{nc}, sy_i^{mc}, sy_i^{fc}$ is used to indicate the symptoms of unvaccinated, during and completed vaccination. This information can be gathered using the record blockchain in the system. The number of these three categories in the city is assumed to be respectively N^n, N^m, N^f . $N^n + N^m + N^f = N.sy_i^c$ indicates the symptoms of the inoculated. Its number is represented by N^c. That is,$N^m + N^f = N^c$.

VE is divided into simple effectiveness (SVE) and comprehensive effectiveness (CVE) (also known as the symptom relief rate). SVE can be further divided into finish vaccination simple effectiveness (FSVE) and comprehensive simple effectiveness (CSVE). CVE can be further divided into finish vaccination comprehensive effectiveness (FCVE) and comprehensive and comprehensive effectiveness (CCVE).

$$FSVE = 1 - \frac{N^n \sum_{i=1}^{N^f} sign\left(sy_i^{fc}\right)}{N^f \sum_{i=1}^{N^n} sign\left(sy_i^{nc}\right)} \quad (1)$$

$$CSVE = 1 - \frac{N^n \sum_{i=1}^{N^c} sign\left(sy_i^{c}\right)}{N^c \sum_{i=1}^{N^n} sign\left(sy_i^{nc}\right)} \quad (2)$$

$$FCVE = 1 - \frac{N^n \sum_{i=1}^{N^f} sy_i^{fc}}{N^f \sum_{i=1}^{N^n} sy_i^{nc}} \quad (3)$$

$$CCVE = 1 - \frac{N^n \sum_{i=1}^{N^c} sy_i^{c}}{N^c \sum_{i=1}^{N^n} sy_i^{nc}} \quad (4)$$

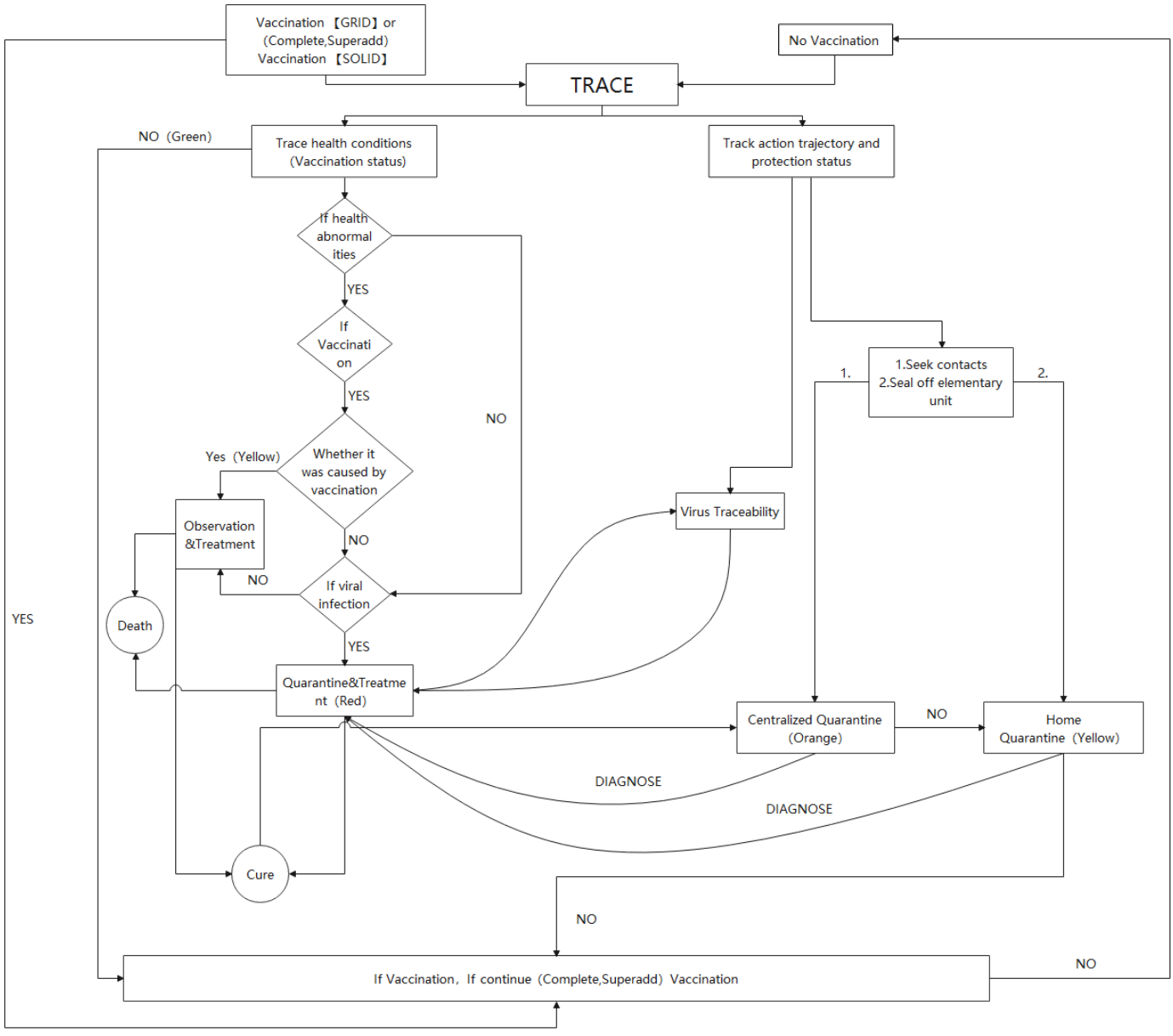

Figure 1 Dynamic Monitoring Model of Urban Vaccine Effectiveness

Figure 1 Dynamic monitoring model of urban vaccine effectiveness.

Group effectiveness and overall effectiveness

In case of epidemic prevention, group division can be divided into two perspectives: one from the perspective of ordinary signs or commonality signs, including age, gender, race, occupation, party, name of vaccination and other signs; and the other one from the perspective of special signs or personality signs, including pregnant women, special diseases, prisoners, nursing homes and other signs. Compound signs can also be used.

For the different groups of people in the city, define the group effectiveness (GVE), calculated separately:

Group FSVE

$$FSGVE_j = 1 - \frac{N^n \sum_{i=1}^{N_j^f} sign\left(sy_{ij}^{fc}\right)}{N_j^f \sum_{i=1}^{N^n} sign\left(sy_i^{nc}\right)} \quad (5)$$

N_j^f indicates the number of group j populations who have completed the vaccination, j=1,2,…,M, same as below.

Group CSVE

$$CSGVE_j = 1 - \frac{N^n \sum_{i=1}^{N_j^c} sign\left(sy_{ij}^{c}\right)}{N_j^c \sum_{i=1}^{N^n} sign\left(sy_i^{nc}\right)} \quad (6)$$

N_j^c indicates the number of group j populations who are vaccinated, j=1,2,…,M, same as below.

Group FCVE

$$FCGVE_j = 1 - \frac{N^n \sum_{i=1}^{N_j^f} sy_{ij}^{fc}}{N_j^f \sum_{i=1}^{N_i^n} sy_i^{nc}} \quad (7)$$

Group CCVE

$$CCGVE_j = 1 - \frac{N^n \sum_{i=1}^{N_j^c} sy_i^{c}}{N_j^c \sum_{i=1}^{N_i^n} sy_i^{nc}} \quad (8)$$

Summarise the GVE to obtain various indicators of the overall effectiveness (OVE).

Overall FSVE

$$FSOVE = \sum_{j=1}^{M} w_j^f FSGVE_j \quad (9)$$

w_j^frepresents the proportion of group j in complete vaccination,$w_j^f = \frac{N_j^f}{N^{fc}}$.

Overall CSVE

$$CSOVE = \sum_{j=1}^{M} w_j CSGVE_j \quad (10)$$

$w_j$represents the proportion of category j in complete vaccination,$w_j = \frac{N_j^c}{N^c}$.

Overall FCVE

$$FCOVE = \sum_{j=1}^{M} w_j^f FCGVE_j \quad (11)$$

Overall CCVE

$$CCOVE = \sum_{j=1}^{M} w_j CCGVE_j \quad (12)$$

Based on the effectiveness of the infectious spatial contact matrix

In Wang and Zhao's study, the health code blockchain was used to establish a spatial contact matrix W reflecting the spatial action trajectory connection between people,[77] and then a spatial contact matrix WH that considers the protection status is introduced. It can even be extended to a connection matrix between different groups. Here, in order to spatially measure VE, the urban infectious spatial contact matrix of COVID-19 is introduced. The elements in the matrix are specifically divided into two forms: one reflects whether it is infected as $WI_t\ (ij)$; and the other one reflects the greatest severity of the infected person as $WS_t\ (ij)$.

For $WI_t\ (ij)$:

$WI_t\ (ii) = 0$indicates that i is not contagious, $WI_t\ (ii) = 1$ indicates that i is contagious.

$$\mathrm{WI}_t\ (ij) = \begin{cases} 0 & i\ do\ not\ pass\ the\ virus\ to\ j \\ 1 & i\ pass\ the\ virus\ to\ j \end{cases}$$

$WS_t\ (ii) = 0$indicates that i is not contagious, and $WS_t\ (ii) = 1, 2, 3, 4$, respectively, represents the four forms of the most severe symptoms that i is infected with.

$$\mathrm{WS}_t\ (ij) = \begin{cases} 0 & i\ do\ not\ pass\ the\ virus\ to\ j \\ 1, 2, 3, 4 & most\ severe\ symptoms\ of\ j\ infected\ by\ i \end{cases}$$

It is defined that:

The unvaccinated vector $NV_{1\times N}$, where each element in the vector is unvaccinated and vaccinated by 1 and 0, respectively, indicates whether the N objects are vaccinated. The vaccination vector $MV_{1\times N}$, where each element in the vector is represented by 1 and 0, respectively, for vaccination and other conditions, indicates whether the N objects are under vaccination. The completed vaccination vector $FV_{1\times N}$, where each element in the vector is represented by 1 and 0, respectively, to complete vaccination and other conditions, indicates whether the N objects have completed the vaccination. The vaccinated vector $NV_{1\times N}$, where each element in the vector is vaccinated and unvaccinated by 1 and 0, respectively, indicates whether the N objects are vaccinated. $E = (1, 1, \cdots, 1)_N$, then $NV_{1\times N} = E - VV_{1\times N}$.

Calculation:

Number of unvaccinated persons=$NV_{1\times N}E^T$

Number of vaccination persons=$MV_{1\times N}E^T$

Number of completed vaccination persons=$FV_{1\times N}E^T$

Number of vaccinated persons=$FV_{1\times N}E^T$

Number of unvaccinated infections=$NV_{1\times N}WI_{N\times N}E^T$

Number of infections during the vaccination=$MV_{1\times N}WI_{N\times N}E^T$

Number of infected persons who completed vaccination=$FV_{1\times N}WI_{N\times N}E^T$

Number of infected people who have been vaccinated=$VV_{1\times N}WI_{N\times N}E^T$

From the perspective of infectious spatial contact matrix, calculate the SVE respectively:

$$FSVE = 1 - \frac{\left(NV_{1\times N}E^T\right)\left(FV_{1\times N}WI_{N\times N}E^T\right)}{\left(FV_{1\times N}E^T\right)\left(NV_{1\times N}WI_{N\times N}E^T\right)} \quad (13)$$

$$CSVE = 1 - \frac{\left(NV_{1\times N}E^T\right)\left(VV_{1\times N}WI_{N\times N}E^T\right)}{\left(VV_{1\times N}E^T\right)\left(NV_{1\times N}WI_{N\times N}E^T\right)} \quad (14)$$

Similarly, calculate the CVE respectively:

$$FCVE = 1 - \frac{\left(NV_{1\times N}E^T\right)\left(FV_{1\times N}WS_{N\times N}E^T\right)}{\left(FV_{1\times N}E^T\right)\left(NV_{1\times N}WS_{N\times N}E^T\right)} \quad (15)$$

$$CCVE = 1 - \frac{\left(NV_{1\times N}E^T\right)\left(VV_{1\times N}WS_{N\times N}E^T\right)}{\left(VV_{1\times N}E^T\right)\left(NV_{1\times N}WS_{N\times N}E^T\right)} \quad (16)$$

According to the infectious spatial contact matrix, the GVE and OVE can be calculated.

Evaluation methods

According to the urban VE dynamic monitoring model established by the health code blockchain, the VE evaluation index system can be used to conduct quantitative and dynamic monitoring of the VE. The specific evaluation methods are divided into vertical evaluation and horizontal evaluation. Longitudinal evaluation can compare non-vaccinated and vaccinated people. In order to more accurately compare the differences between the two groups in the city, the propensity value matching analysis method can be used to find samples with similar population characteristics from non-vaccinators and vaccinators for comparison. Horizontally, statistical methods such as sequential analysis can be used to dynamically monitor and test whether the VE evaluation index reaches a certain standard or exceeds the warning level.

Find patient zero and asymptomatic patients

Using the urban spatial contact matrix considering protection status WH, patient zero and relevant asymptomatic

patients can be identified according to the first confirmed patient. The algorithm principle is as follows:

Assuming that urban $WH_t(ij)$ is known, $t \in [0,T]$, and $WH_T(ii)$ =1 (unprotected) or 0 (protected).

1. tb=0 te=d/Set tb, te to time backtracking start and end variables, respectively, and d is usually selected for a length of infectious infection time/.
2. h=tb to te.
3. j=1 to N.
4. Find all $WH_{T-h}(ij)$ = 1/Find all j, equal to 1 in the $WH_{T-h}(ij)$, namely {j}/.
5. $j \rightarrow J$/Enter information about j including vaccination into the database J/.
6. End j.
7. i={j}/All j's will be found as the i for the next loop/.
8. End h.
9. All persons in the data set J are isolated and nucleic acid tested.
10. If no positive is found, then tb=te + 1 te=te + d go to 2 until positive is found or t=0/If no positive is found, it indicates other ways such as COVID-19 transmission through input items/.
11. If positive is found (the earliest positive (usually asymptomatic) may be patient zero), then find all unprotected contacts and their sequential unprotected contacts from the positive person traced back until the end of the T moment.
12. These unprotected contacts are centrally isolated and nucleic acid tested for positive.
13. The unprotected contact is positive for nucleic acid monitoring before T time, indicating asymptomatic; if positive after T time, there are two situations: asymptomatic and symptomatic.

In $WH_t(ij)$, i and j adopt anonymous identifiers. After finding patient zero and asymptomatic patients, according to the pre-established personal identity dynamic anonymous identifier and use key database, the true identity is restored with the use key according to the authorisation.

The above algorithm can trace the city patient zero and asymptomatic patients, and analyse the differences between patient infection to vaccinated and unvaccinated persons, as well as the distribution, intergenerational differences and development trends of asymptomatic patients in early stage of the urban epidemic.

Monitoring and statistical evaluation of the personal privacy information use

Based on the classification of personal privacy information, the special supervision organisation shall track and monitor the use of personal privacy information by relevant institutions in the system in all time and space, count the amount of privacy information used, including normal use and illegal use (including disclosure), and evaluate the possible harm caused by illegal use (including disclosure) of privacy information.

Privacy information classification

According to the needs of epidemic prevention and control, the personal information (pi) in the system can be divided into three levels (0–2) from the perspective of the degree of personal interest connection. The first level is non-privacy information, and the pi value is 0, including individual gender and age, protection status, vaccination and other information. The second level is low privacy information, with pi value of 1, including personal action trajectory, telephone and other information. The third level is high private information, with pi value of 2, including personal identity, residence, health and other information.

Statistical evaluation indicators

Normal usage of privacy information

$$NSPI = \sum_{i=1}^{N} \left(\sum_{j=1}^{M} pi(ij)\, NF(ij) \right) \tag{17}$$

i from 1 to N represents the number of people, j from 1 to M represents the number of types of information and $NF(ij)$ represents the number of normal uses of type j information of the ith individual.

Illegal usage of privacy information

$$ISPI = \sum_{i=1}^{N} \left(\sum_{j=1}^{M} pi(ij)\, IF(ij) \right) \tag{18}$$

$IF(ij)$represents the number of illegal uses of type j information of ith individual.

Proportion of illegal use of privacy information

$$NISPI = \sum_{i=1}^{N} \sum_{j=1}^{M} sign(pi(ij))\, IF(ij) \,/\, \sum_{i=1}^{N} \sum_{j=1}^{M} sign(pi(ij))\, (NF(ij) + IF(ij)) \tag{19}$$

Intensity of illegal use of privacy information

$$IISPI = ISPI/(NSPI + ISPI) \tag{20}$$

Application of statistical analysis

Evaluate the VR and determine the optimal vaccination strategy

The VR is usually reflected by the proportion of the total population. We believe that the proportion of the vaccination population alone does not accurately reflect the effect of the vaccination. Let us analyse a typical vaccination case.

Referring to the practice of Wang and Zhao,[77] a representative city is composed of three regions (ABC), in which A region consists of two subregions 1 and 2, B region consists of two subregions 3 and 4 and C region consists of two subregions 5 and 6. From the perspective of regional orientation and function in the city, the A area is equivalent to the far urban area (or suburbs) of the city, the subregion 1 is equivalent to the rural or small town, the subregion 2 is equivalent to the central town in it and the B and C areas are equivalent to the central urban area, among which B is more prominent than C in the centre of the city. The spatial contact matrix obtained from the health code blockchain is shown below, in which all the partitioned matrices with subscripts are not 0. If six subregions in the region are regarded as network nodes, it is not difficult to see that the node degree of subregion 3 is 4, the highest; second, the node degree of subregion

Table 3 Comparison table of different vaccination programmes

Programme	First vaccination subregion	Second vaccination subregion	Number of effective protection block matrices for the first vaccination	Proportion in the total number of block matrices (%)
1	1 3 5	2 4 6	17	85
2	1 3 6	2 4 5	15	75
3	1 4 5	2 3 6	14	70
4	1 4 6	2 3 5	13	65
5	2 3 5	1 4 6	17	85
6	2 3 6	1 4 5	15	75
7	2 4 5	1 3 6	15	75
8	2 4 6	1 3 5	15	75

5 is 3, again subregions 2, 4 and 6 are 2, subregion 1 is 1 and the minimum.

It is further assumed that the same number of people per subregion is equal and the cumulative sum of all elements in each WH block matrix is equal. Suppose that a vaccination plan is now to be determined. Routine practices synchronise vaccination across all regions, assuming that a subregion is selected for vaccination in each region and then in the remaining subregion. There are eight programmes (see table 3). In terms of the proportion of the vaccination population, the eight programmes have the same VR, all equal to 60%, but the actual effect is different.

Programme 1 first selects three subregions (1, 3, 5) in the ABC regions for vaccination (table 3). In the six regions, from the perspective of mobility (or spatial contact), subregion 3 vaccination provides the best protection effect, which provides vaccination protection for the own population, and provides immune protection for the four subregions (2, 4, 5, 6). The protective effect of subregion 5 vaccination is the second best. It provides inoculation protection for its own population, and provides immune protection for the three subregions (3, 4, 6). The protective effect of subregion 1 vaccination is the worst, which can only provide immune protection for one subregion 2 while providing vaccination protection for its own population. The whole protection effect of the three subregions of 1, 3 and 5 vaccination covers 17 block (spatial contact) matrices, accounting for 85% of all 20 block matrices. This protection effect is the same as programme 5 and all are optimal in all eight programmes. Programme 4 has the worst protection effect, with only 65%.

$$\begin{vmatrix} WH_{11} & WH_{12} & 0 & 0 & 0 & 0 \\ WH_{21} & WH_{22} & WH_{23} & 0 & 0 & 0 \\ 0 & WH_{32} & WH_{33} & WH_{34} & WH_{35} & WH_{36} \\ 0 & 0 & WH_{43} & WH_{44} & WH_{45} & 0 \\ 0 & 0 & WH_{53} & WH_{54} & WH_{55} & WH_{56} \\ 0 & 0 & WH_{63} & 0 & WH_{65} & WH_{66} \end{vmatrix}$$

This shows that the same proportion of people vaccinated will not get the same effect. This is due to the uneven mobility of the population, which is closely associated with the spread of the virus, and the consequent uneven connections between people. A large number of facts prove that high mobility leads to a high spread of the virus. Personnel mobility can be considered from three aspects: one is the flow intensity (ie, the flow frequency), the second is the breadth of the flow range, the third is the flow contact width (ie, the number of contacts). Different mobility brings different effects of virus transmission. Therefore, the measurement of population VR should be divided into whether to consider population mobility, without considering population mobility as simple vaccination rate (SVR), considering population mobility as comprehensive vaccination rate (CVR), which means that indicators reflecting population mobility are weighted to calculate the effectiveness of vaccination, and those vaccinated are weighted.

The index will soon reflect population mobility as the weight to calculate the effectiveness of vaccination, and weighted the vaccinators. Here, the element of spatial contact matrix $W(ij)$ is used as a representative indicator of personnel mobility, namely:

$$CVR = \left(\sum_{i=1}^{N}\sum_{j=1}^{N} W(ij)\, I(i)\right) / \left(\sum_{i=1}^{N}\sum_{j=1}^{N} W(ij)\right), \quad (21)$$

where $I(i)$ is the indicator function of whether i is vaccinated, vaccinated equal to 1 and unvaccinated equal to 0.

The sequence of vaccination to the general population should be based on population mobility. Its optimal strategy is:

1. First, vaccinate the high-mobility group (high-mobility areas).
2. In the remaining groups (regions), select the group (region) that has no association with (1) group (region) but has the largest association with the remaining groups (regions) for vaccination. If the same exists, select the group (region) with more contacts. If still the same, the larger group (the middle region) is chosen.
3. And so on, until all groups (regions) are vaccinated.

If the above ABC regions adopt the overall subregion gradual vaccination method, the optimal vaccination order is 3-5-2-4-6-1 according to the optimal vaccination strategy principle.

Evaluate herd immunity

It is the most effective way to deal with the epidemic situation of COVID-19 at present by large-scale vaccination, achieving herd immunity and providing protection for vaccinated and unvaccinated persons. According to existing views, the basic reproduction number under herd immunity is equal to R0*(1-VR*VE), if protection status is not considered. The herd immunity means that the VR must meet the above formula less than 1. This analysis logic is mainly aimed at the situation of symptomatic infected person: when the infected person has symptoms, it means that the transmission path is cut-off, and the action time of herd immunity is from its incubation period with the infectious ability to the time of onset. Usually, asymptomatic is divided into two types: invisibility and incubation, of which invisibility accounts for a large proportion.[78 79] This study mainly refers to invisibility. In the case of asymptomatic persons, the transmission path can be cut only when symptoms appear in the second generation of their infection: that is, asymptomatic persons can be infected from the incubation period when they have the ability to infect until the onset of symptoms in the second generation, and the whole second generation will also spread from the time they have the ability to infect until the onset of symptoms in the symptomatic ones. Asymptomatic patients have altered the original epidemic transmission model (SEIR (Susceptible-Exposed-Infected-Removed)).[80] This means that for asymptomatic person, herd immunity protects against a wider range of infections and for a longer period of time, thus requiring a higher rate of vaccination. Below, the relevant urban simulation is given:

Assumption 1. The proportion of asymptomatic and symptomatic persons (including incubation-type asymptomatic patients who become symptomatic) is aw and 1-aw, respectively; and it is assumed that this proportion is fixed in different generations of virus transmission.[81]

Assumption 2: The symptomatic and asymptomatic persons carry the same amount of poison, that is, the number of infections per unit time is the same, and the duration of infection is the same.[82]

Assumption 3: The symptomatic and asymptomatic persons have the same incubation period (ip) and are contagious on the last k days of the incubation period.

Assumption 4: Epidemic prevention and control is carried out in accordance with the traditional epidemiological investigation combined with local full nucleic acid testing and screening. That is：

1. For symptomatic patients, once the disease occurs, find their contacts through epidemiological investigation for isolation and nucleic acid detection to block the transmission.
2. For asymptomatic patients, once the second generation of symptomatic patients is found, the asymptomatic patients, other second-generation infected persons and their contacts shall be identified through epidemic investigation, combined with local nucleic acid testing and screening, and these persons shall be isolated and nucleic acid detection to block the transmission.[83]

Assumption 5: The vaccination rate of the whole population is VR. For symptomatic and asymptomatic persons, the VE (ie, SVE) in preventing infection is the same.

Thus:

For symptomatic person, the basic reproduction number under herd immunity is:

$$R^s = R0^s\left(1 - VRVE\right) \tag{22}$$

The $R0^s$ is equal to the commonly considered R0.

For asymptomatic people, the basic reproduction number under herd immunity is:

$$R^a = R0^s\left(1 - VRVE\right)\frac{(ip+1)}{(k+1)} + \left(R0^s\left(1 - VRVE\right)\right)\text{^}2 \tag{23}$$

To sum up, the comprehensive basic reproduction number under herd immunity is:

$$R = \left(1 - aw\right)R^s + awR^a$$
$$= \left(1 - aw\right)R0^s\left(1 - VRVE\right) + aw(R0^s(1 - VRVE)\frac{(ip+1)}{k+1} + (R0^s(1 - VRVE))\text{^}2) \tag{24}$$

It is not difficult to see from the formula that the R is proportional to aw and ip, and is inversely proportional to VR, VE and k. From the simulation results (table 4), if not asymptomatic, the R rapidly decreases to 1.08 and 1.8 under herd immunity when the VR reaches 80% and R0 is 3 and 5, respectively. However, due to asymptomatic existence, the R is still high, even at the 80%, even when the asymptomatic population reaches a certain proportion (symptomatic R0=3, aw=0.65; symptomatic R0=5,

Table 4 Simulation of the comprehensive basic reproduction number

$R0^s$=3, VR=0.8, VE=0.8, ip=7, k=2							
aw	0.2	0.3	0.4	0.5	0.6	0.7	0.8
R	1.6733	1.9699	2.2666	2.5632	2.8598	3.1565	3.4531
$R0^s$=5, VR=0.8, VE=0.8, ip=7, k=2							
aw	0.2	0.3	0.4	0.5	0.6	0.7	0.8
R	3.0480	3.6720	4.2960	4.92	5.544	6.1680	6.7920

ic, incubation period; VE, vaccine effectiveness; VR, vaccination rate.

aw=0.52), the R will exceed the original R0. When symptomatic R0=3, even with aw=0.2, the R decreases to nearly 1 until the VR reaches 95%. When aw=0.8, even when the entire population is vaccinated, namely VR=1, the R is 1.688, and is still significantly greater than 1. If the R is to be reduced to 1, the VE needs to be increased to 0.87.

From the simulation analysis, the R can more accurately reflect the effect of herd immunity than the traditional R0*(1-VR*VE) in the presence of asymptomatic cases. In the simulation analysis, in order to find asymptomatic patients in the city and block their transmission, it is necessary to introduce nucleic acid testing for all local people and screening with high cost and loss. If the monitoring, evaluation and application system in this paper is used, whether the first generation of symptoms appears (found), or the second generation of symptoms appears (found), we do not need to take local full nucleic acid testing and screening, just through the traceability of contact personnel can we quickly and easily find the asymptomatic and potential infected persons, so as to better play the role of herd immunity.

Monitor the VE on variant

In order to make the monitoring, evaluation and application system established in this paper, monitor the impact of variation on urban VE in real time, we at first need to expand the monitoring model, in the 'If viral infection' judgement diamond box along the 'yes' arrow to add a 'whether variant virus infection' judgement diamond box, and then through two 'yes' and 'no' path arrows to 'Quarantine&Treatment (Red)' box, and set special monitoring variables to reflect the holder infected with variant virus.

Assuming that the COVID-19 mutates at some time in the city, the monitoring, evaluation and application system can be used to track the transmission of the variant virus among the holders, so that information about all the infected persons can be collected in a comprehensive and timely manner, including their contact groups, the inoculation status of these groups and the infection status of these groups. The traditional epidemic investigation cannot fully and accurately trace contacts of infected persons, and some contacts of infectious persons have not been observed, that is to say, the loss of contacts is inevitable. Since there is a large number of asymptomatic people among both the infected persons and their contacts, the loss will be aggravated.[84–86] Variant viruses often change the mode of transmission, and enhance the intensity and speed of transmission. This further aggravates the loss if the traditional investigation is continued for use. Below, we compare the differences between the monitoring, evaluation and application system and the traditional epidemic investigation in monitoring the impact of viral variants on urban VE.

The monitoring, evaluation and application system would collect the contacts of each person infected with the variant virus for classification statistics. First, the contacts are divided into whether they are infected or not, and then into whether they could be observed by the traditional epidemic investigation. The supermark of the variable is 1 to indicate that they are observed, and 0 to indicate that they could not be observed. The third subdivision is further divided according to the inoculation status, and the results are shown in table 5. It is assumed that the protection status is not considered here. The contact personnel classification statistics of all infected persons are summarised to obtain the overall situation of the contacts.

FSVE represents the true SVE of completed vaccination against the variant virus (hereinafter referred to as true effectiveness), and $FSVE^1$ represents the SVE of completed vaccination observed in the current epidemic investigation (hereinafter referred to as observed effectiveness).

$$FSVE = 1 - \frac{\sum_{i=1}^{N}\left(tpny_i^1+tpny_i^0+tpnn_i^1+tpnn_i^0\right)*\sum_{i=1}^{N}\left(tpfy_i^1+tpfy_i^0\right)}{\sum_{i}^{N}\left(tpfy_i^1+tpfy_i^0+tpfn_i^1+tpfn_i^0\right)*\sum_{i=1}^{N}\left(tpny_i^1+tpny_i^0\right)} \quad (25)$$

$$FSVE^1 = 1 - \frac{\sum_{i=1}^{N}\left(tpny_i^1+tpnn_i^1\right)*\sum_{i=1}^{N} tpfy_i^1}{\sum_{i=1}^{N}\left(tpfy_i^1+tpfn_i^1\right)*\sum_{i=1}^{N} tpny_i^1} \quad (26)$$

N represents the number of infected persons. It is not excluded that there is overlap between the contacts of each infected person, and the amount of overlap should be eliminated when summarised.

Whether the observed effectiveness is consistent with the true effectiveness depends on whether the structure of the unvaccinated group and the completed group of the infected person's contacts is the same between the observed and the unobserved. Let us discuss some typical cases.

1. The structure is identical.

$$tpny_1^0 = k * tpny_i^1, tpnn_i^0 = k * tpnn_i^1; tpfy_i^0 = k * tpfy_i^1; tpfn_i^0 = k * tpfn_i^1; k > 0 \quad .$$

Table 5 Classification statistics of contacts of variant virus infected person i

Whether infected	Whether observed by epidemic investigation	Contact number (tp)	Number of unvaccinated (tpn)	Number of vaccinated (tpm)	Number of completed vaccination (tpf)
Yes	Yes	tpy_i^1	$tpny_i^1$	$tpmy_i^1$	$tpfy_i^1$
	No	tpy_i^0	$tpny_i^0$	$tpmy_i^0$	$tpfy_i^0$
No	Yes	tpn_i^1	$tpnn_i^1$	$tpmn_i^1$	$tpfn_i^1$
	No	tpn_i^0	$tpnn_i^0$	$tpmn_i^0$	$tpfn_i^0$

There is $FSVE = FSVE^1$.

2. The unvaccinated contacts and the completed vaccinated contacts of each infected person have the same internal structure and different structure from each other.

$$tpny_i^0 = k_1 * tpny_i^1, tpnn_i^0 = k_1 * tpnn_i^1; tpfy_i^0 = k_2 * tpfy_i^1; tpfn_i^0 = k_2 * tpfn_i^1$$
$$k_1 > 0, k_2 > 0, k_1 \neq k_2.$$

There is still $FSVE = FSVE^1$.

3. The unvaccinated contacts and the completed contacts of all infected persons have the same internal structure and a different structure from each other.

$$\sum_{i=1}^{N} tpny_i^0 = k_1 * \sum_{i=1}^{N} tpny_i^1, \sum_{i=1}^{N} tpnn_i^0 = k_1 * \sum_{i=1}^{N} tpnn_i^1;$$
$$\sum_{i=1}^{N} tpfn_i^0 = k_2 * \sum_{i=1}^{N} tpfn_i^1, \sum_{i=1}^{N} tpfn_i^0 = k_2 * \sum_{i=1}^{N} tpfn_i^1$$
$$k_1 > 0, k_2 > 0, k_1 \neq k_2.$$

There is still $FSVE = FSVE^1$.

4. The internal structure of unvaccinated contact groups and vaccinated contact groups of all infected persons is not balanced.

Let us look at the case where high population proportions are not observed.

Specific analysis of four cases:

Case 1: The number of unvaccinated persons is large and the variant virus is not highly contagious, and the unobserved proportion of unvaccinated people who are not infected is higher.

Assume the unvaccinated rate of 0.8, the ongoing VR of 0.1, the completed VR of 0.1 and an average infection rate of 2% for the variant virus. The effect of observed effectiveness is simulated by showing that the proportion of unobserved persons ($tpnn^0$) in the unvaccinated population who are not infected is higher in two situations of true effectiveness of 90% and 80%, respectively (table 6). We find that the higher the unobserved proportion of unvaccinated people who are not infected, the greater the overestimate of observed effectiveness and the greater the gap from true effectiveness. For example, if a vaccine is more than 90% effectiveness against the premutant virus, but only 80% effectiveness against the mutant virus, and because 80% of the unvaccinated people who are not infected are not observed, the observed effectiveness of the vaccine is 91.76%, it will lead to the wrong judgement that the VE against the variant virus is not decreased.

Table 6 Simulation of case 1 with true effectiveness of 90% and 80%, respectively

$tpnn^0$ (%)	0.5	0.6	0.7	0.8	0.9
FSVE	0.9	0.9	0.9	0.9	0.9
$FSVE^1$	0.9	0.9196	0.9392	0.9588	0.9784
$tpnn^0$ (%)	0.5	0.6	0.7	0.8	0.9
FSVE	0.8	0.8	0.8	0.8	0.8
$FSVE^1$	0.8	0.8392	0.8784	0.9176	0.9568

It is assumed that the proportion of the unobserved and observed people in the infected unvaccinated, the infected with complete vaccination and the uninfected with complete vaccination is the same.

Table 7 Simulation of case 2 with true effectiveness of 90% and 80%, respectively

$tpny^0$ (%)	0.5	0.6	0.7	0.8	0.9
FSVE	0.9	0.9	0.9	0.9	0.9
$FSVE^1$	0.9	0.8763	0.8367	0.7575	0.52
$tpny^0$ (%)	0.5	0.6	0.7	0.8	0.9
FSVE	0.8	0.8	0.8	0.8	0.8
$FSVE^1$	0.8	0.7525	0.6733	0.515	0.04

It is assumed that the proportion of the unobserved and observed people in the uninfected unvaccinated, the infected with complete vaccination and the uninfected with complete vaccination is the same.

Case 2: The number of unvaccinated persons is large and the variant virus is highly contagious, and the proportion of unvaccinated people who are infected is high.

Assume the unvaccinated rate of 0.8, the ongoing VR of 0.1, the completed VR of 0.1 and an average infection rate of 5% for the variant virus. The effect of observed effectiveness is simulated by showing that the proportion of unobserved persons ($tpny^0$) in the unvaccinated population who are infected is higher in two situations of true effectiveness of 90% and 80%, respectively (table 7). We find that the higher the proportion of unvaccinated infected people who are not observed, the lower the estimate of observed effectiveness; and the lower the true effectiveness, the larger the gap between observed effectiveness and true effectiveness.

Case 3: The number of vaccinated persons is large and the variant virus is not highly contagious, and the unobserved proportion of completed vaccination people who are not infected is higher.

Assume the unvaccinated rate of 0.2, the ongoing VR of 0.2, the completed VR of 0.6 and an average infection rate of 2% for the variant virus. The effect of observed effectiveness is simulated by showing that the proportion of unobserved persons ($tpfn^0$) in the completed vaccination population who are not infected is higher in two situations of true effectiveness of 90% and 80%, respectively (see table 8). We find that the higher the proportion of unobserved completed vaccination patients who are not infected, the lower the estimate of observed effectiveness; and the lower the true effectiveness, the larger the gap between observed effectiveness and true effectiveness.

Case 4: The number of vaccinated persons is large and the variant virus is highly contagious, and the unobserved proportion of completed vaccination people who are infected is higher.

Assume the unvaccinated rate of 0.2, the ongoing VR of 0.2, the completed VR of 0.6 and an average infection rate of 5% for the variant virus. The effect of observed effectiveness is simulated by showing that the proportion of unobserved persons ($tpfy^0$) in the completed vaccination population who are infected is higher in two situations of

Table 8 Simulation of case 3 with true effectiveness of 90% and 80%, respectively

$tpfn^0$ (%)	0.5	0.6	0.7	0.8	0.9
FSVE	0.9	0.9	0.9	0.9	0.9
$FSVE^1$	0.9	0.8751	0.8336	0.7507	0.5040
$tpfn^0$ (%)	0.5	0.6	0.7	0.8	0.9
FSVE	0.8	0.8	0.8	0.8	0.8
$FSVE^1$	0.8	0.7502	0.6676	0.5030	0.0157

It is assumed that the proportion of the unobserved and observed people in the uninfected unvaccinated, the infected unvaccinated and the infected with complete vaccination is the same.

true effectiveness of 90% and 80%, respectively (table 9). The infected persons who have completed the vaccination are not observed, and may be asymptomatic or symptomatic. For symptomatic patients, there is no report or discovery, which may be subjective concealment or objective mistake believing other diseases such as cold. We find that the higher the unobserved proportion of infected completed vaccinators, the greater the overestimate of observed effectiveness and the greater the gap from true effectiveness. For example, if a vaccine is more than 90% effectiveness against the premutant virus, but only 80% effectiveness against the mutant virus, and because 80% of the infected people with complete vaccination are not observed, the observed effectiveness of the vaccine is 91.95%; similar to case 1, it will lead to the wrong judgement that the VE against the variant virus is not decreased.

In brief, regardless of the relatively high unobserved proportion of the above four cases, it will directly lead to the obvious deviation of the observed effectiveness from the real effectiveness. For cases 2 and 3, the lower the true effectiveness, the greater the deviation. For cases 1 and 4, the higher the true effectiveness, the greater the deviation, and both produce wrong judgements that the VE against the variant virus is not decreased.

Patient and public involvement

This study did not involve specific patients and the public.

Table 9 Simulation of case 4 with true effectiveness of 90% and 80%, respectively

$tpfy^0$ (%)	0.5	0.6	0.7	0.8	0.9
FSVE	0.9	0.9	0.9	0.9	0.9
$FSVE^1$	0.9	0.9199	0.9399	0.9599	0.9799
$tpfy^0$ (%)	0.5	0.6	0.7	0.8	0.9
FSVE	0.8	0.8	0.8	0.8	0.8
$FSVE^1$	0.8	0.8397	0.8795	0.9195	0.9597

It is assumed that the proportion of the unobserved and observed people in the uninfected unvaccinated, the infected unvaccinated and the uninfected with complete vaccination is the same.

RESULTS

System analyses

This study uses the health code blockchain platform, and combines with the listed VE dynamic monitoring model, the VE evaluation index system and the monitoring and evaluation system of personal privacy information use to build the urban COVID-19 VE monitoring, evaluation and application system. The system organically combines centralised management with decentralised technology by using blockchain technology, combines the tracking of individual vaccine action information with his or her action trajectory information and implements the principles of 'privacy information available but invisible' and 'tolerating the lack of information', which dynamically monitor and accurately evaluate the effectiveness of the vaccines in all aspects, all processes and all time and space, comprehensively and truly trace the action trajectory of the vaccines and maximise the privacy of individuals, without locking down the relevant area or the city. Its remarkable characteristics are as follows. First, build a complete vaccination-related information management system with relative division of labour and mutual restriction through the hierarchical decentralisation of roles. Second, ensure complete traceability of the construction and use of vaccination-related information by building two types of blockchains (the record blockchains and the use blockchains). Third, use smart contracts to carry out information management, use and scene application of holder VE, to ensure that the use of holder information is implemented in accordance with the predetermined way and content norms. The system can find the city patient zero and asymptomatic patients, and analyse the differences between patient infection to vaccinated and unvaccinated persons.

Simulation analyses

According to this system, combined with simulation and other methods, it is found that: (1) The measurement of VRs should be combined with urban population mobility: the same proportion of the vaccination population has different vaccination results under the mobility of different populations. The weighted CVRs, which are calculated by taking indicators of population mobility as a weight, are more accurate than SVRs without account of population mobility. It is believed that the urban optimal vaccination strategy should be determined based on population mobility, and the principle of the urban optimal vaccination algorithm is given. (2) In the presence of asymptomatic conditions, the basic reproduction number, namely R0*(1-VR*VE), does not accurately reflect the effect of herd immunity, but the comprehensive basic reproduction number (R) should be used. The R is directly proportional to the proportion of asymptomatic people and the duration of the incubation period, and inversely proportional to the VR, the VE and the number of days transmitted in the incubation period. When the proportion of asymptomatic is high, even if all urban persons are vaccinated, the R can still

be significantly greater than 1. To reduce the R to below 1, further improving the effectiveness of the vaccines is needed. If VE is difficult to improve, measures such as enhanced protection should be taken to reduce R. (3) Compared with the traditional epidemiological investigation, the monitoring, evaluation and application system in this study as an active dynamic tracking mode can more accurately grasp the impact of the variant virus on urban VE. Unlike the monitoring, evaluation and application system, which can fully grasp the contacts of infected persons, the traditional epidemiological investigation can produce the situation that the contacts are not observed, and lead to the deviation between the observed effectiveness and the true effectiveness. Virus variation aggravates the unobserved situation, and then increases the deviation. The higher the proportion of unobserved personnel, the greater the deviation. When a large number of people are vaccinated, the variant virus is highly contagious, and the unobserved proportion of completed vaccination people who are infected is higher, the wrong judgement that the VE against the mutation virus is not decreased would occur.

DISCUSSION

Based on the above analysis, it is not difficult to summarise the differences between the health code blockchain method established in this paper and the traditional epidemiological investigation method in the monitoring and evaluation of the effectiveness of listed vaccines (table 10). Obviously, this VE monitoring, evaluation and application system needs to be supported by strong financial resources, complete information system, sufficient nucleic acid testing conditions, strong organisation and public understanding. The effectiveness of the vaccines is related to both the vaccination factors and the development of the epidemic. Therefore, the use of this system should adapt to the stage and environment of the development of the city epidemic, and consider many of the above supporting factors of the system, especially cost. This requires comprehensive consideration from the aspects of monitoring cost (MC) and monitoring fine granularity (MFG) (including monitoring range (MS), monitoring depth (MD) and monitoring frequency (MF)). MC is proportional to MFG:

$$MC \sim MFG = MSMDMF \tag{27}$$

For urban in the outbreak period, in view of the characteristics of fast spread and wide coverage of epidemic, the monitoring should adopt the way of full round, full depth and high frequency, whose purpose is to enhance the fine granularity of monitoring, so as to accurately quantify the effectiveness of the vaccines. For urban in the stable control period, there are usually two different situations: one is the sudden sporadic and wide distribution situation, monitoring can adopt full-round, low-depth and low-frequency mode; the other one is the local large-area outbreak but no diffusion, monitoring can use the full-round, full-depth and high-frequency methods in burst areas, and all-round, low-depth and low-frequency methods in non-burst areas.

The use of some existing monitoring means and tools, such as the collection of mobile phone Global Positioning System signals, credit card transaction data and monitoring lens records of confirmed patients in South Korea, is helpful to improve the implementation efficiency of the system and reduce the MC.[87]

Policy implications

Infectious diseases are considered by many experts as the number one threat to human beings in the 21st century. The COVID-19 pandemic seems to confirm this view. As a powerful weapon for tackling infectious diseases, the development and use of vaccines must adapt to the development trends and new characteristics of infectious diseases.[88 89] Traditionally, vaccine development and listing are relatively independent and have long time cycles for both. But the COVID-19 outbreak presents the new characteristics of fast outbreak, fast spread, fast variation, more asymptomatic, easy to repeat, unpredictable,[90] and therefore forces vaccine development and use to change the traditional 'slow pace' mode, take 'treat fast with fast' and 'using space to win time', combine the development and listing, focus on listing as soon as possible for vaccine development and speed up development in the public use. Therefore, it is particularly important to monitor and evaluate the effectiveness of 'emergency' listed vaccines. It can be predicted that infectious diseases will be more powerful and more deadly than COVID-19 in the future. For the future, it is more strategic and valuable to establish a normalised all-aspect, all-process and all-time and space monitoring and evaluation system for effectiveness of listed vaccines.

This study shows that an urban listed VE monitoring, evaluation and application system can be established by using the health code blockchain technology. This system can be used to comprehensively monitor and prevent the development of urban epidemic. This system can enable more accurate monitoring and evaluation of the effectiveness of listed vaccines, meet people's personalised needs for vaccination and promote vaccine improvement. The system could serve as a universal template for cities around the world. If this system can be promoted globally, it will promote countries to strengthen unity and cooperation and enhance the global ability to respond to COVID-19.

The establishment of the system is an extremely arduous task for the urban and faces many challenges: it depends on the development of blockchain technology and large capital investment, more depends on whether the urban managers and medical staff agree on the concept, as well as the coordination of many relevant departments and units in the urban, and depends on the understanding, support and cooperation of the general public. But faced with the deadly threat brought by epidemics such as COVID-19, the urban government must take the lead in this regard.

Table 10 Comparison between traditional methods of epidemic investigation and health code blockchain method in monitoring and evaluating the effectiveness of listed vaccines

Compare content	Traditional methods	Health code blockchain methods
Investigation mode.	Small data.	Big data.
Organisation system.	Mainly involving public health, medical and related research institutions.	Led by government and participated by relevant institutions of the whole society.
Investigation method.	Traditional methods (including sampling survey, telephone survey, etc).	Both traditional methods and modern methods (including big data methods and blockchain methods).
Relationship between epidemic prevention and control and VE monitoring and evaluation.	Relatively independent.	Merge into one.
Methods and effects of tracing the transmission path and source of the virus.	Ex post facto, difficult to fully trace.	Focus on ex ante and in-process tracing, can be fully traced.
Scope of the respondents and the number of omissions.	Incomplete, there may be many omissions in the statistics of confirmed patients and their contacts.	Almost complete, there are few omissions in the statistics of confirmed patients and their contacts.
Requirements for the degree of cooperation of the respondents.	General.	High.
Quantity and quality requirements for investigators.	The quantity is relatively small and the quality is relatively low.	The quantity is relatively large and the quality is relatively high.
The investigator knows the privacy of the respondent.	Relatively more comprehensive.	According to the emergency degree of the antiepidemic state, conditional know.
Do respondents know how their privacy information is being used?	Unknown.	Known.
Whether there is illegal use and disclosure of the respondent's privacy.	Yes, more likely.	Yes, less likely.
Capital investment.	More.	A great many.
Requirements for cooperation with all aspects of society.	Not high.	High.
Accuracy of VE monitoring and evaluation.	Limited to specific groups controlled by public health and medical institutions, there may be errors.	For all the people, more accurate.
Time delay of VE monitoring and evaluation.	Obvious lag.	Basic synchronisation.
Impact of VE monitoring and evaluation on public life.	Not big.	Bigger.
Impact of virus variation on VE monitoring and evaluation.	Not easy to control, the observed results may deviate from the actual results.	Ability to control, the observed results are in agreement with the actual results.
Impact of asymptomatic infection on VE monitoring and evaluation.	Not easy to control, the observed results may deviate from the actual results.	Ability to control, the observed results are in agreement with the actual results.
Requirements for remedial action.	May occur frequently, with high remedial requirements and longer periods.	Less likely to occur.

VE, vaccine effectiveness.

CONCLUSIONS

Compared with traditional epidemiological investigation, this system established in this study can meet the challenges of accelerating virus variation and a large number of asymptomatic people, dynamically monitor and accurately evaluate the effectiveness of listed vaccines and maximise personal privacy without locking down the relevant area or city. This system could serve as a universal template for monitoring and evaluating the effectiveness of COVID-19 listed vaccines in cities around the world.

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REFERENCES

1 Bartsch SM, O'Shea KJ, Ferguson MC, *et al*. Vaccine efficacy needed for a COVID-19 coronavirus vaccine to prevent or stop an epidemic as the sole intervention. *Am J Prev Med* 2020;59:–:493–503.
2 Galanti M, Pei S, Yamana TK, *et al*. Non-pharmaceutical interventions and inoculation rate shape SARS-CoV-2 vaccination campaign success. *Epidemiol Infect* 2021;149:1–8.
3 Storlie CB, Pollock BD, Rojas RL, *et al*. Quantifying the importance of COVID-19 vaccination to our future outlook. *Mayo Clin Proc* 2021;96:1890–5.
4 Huan Y, Bi Y. Research progress and prospect of vaccines for the coronavirus disease 2019 (COVID-19) (in Chinese). *Sci Sin Vitae* 2021;51.
5 Qian X, Wang R, Zhao P. Progress in Novel Coronavirus vaccine research (in Chinese). The PLA Medical Journal 2021;46(07):710-717. Available: https://kns.cnki.net/kcms/detail/11.1056.R.20210616.1003.002.html [Accessed 1 Sept 2021].
6 How many brands of COVID-19 vaccine are available? there are five specific brands of COVID-19 vaccine in China! (in Chinese). Available: https://www.tuliu.com/read-132356.html [Accessed 15 Mar 2022].
7 Zhang Z, SP W, Liu YW. Aerosolized Ad5-nCoV booster vaccination elicited potent immune response against the SARS-CoV-2 omicron variant after inactivated COVID-19 vaccine priming. *medRxiv* 2022.
8 Polack FP, Thomas SJ, Kitchin N, *et al*. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020;383:2603–15.
9 Baden LR, El Sahly HM, Essink B, *et al*. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med* 2021;384:403–16.
10 Doria-Rose N, Suthar MS, Makowski M, *et al*. Antibody persistence through 6 months after the second dose of mRNA-1273 vaccine for Covid-19. *N Engl J Med* 2021;384:2259–61.
11 Voysey M, Clemens SAC, Madhi SA, *et al*. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet* 2021;397:99–111.
12 Alimehmeti I. Efficacy and safety of AZD1222, BNT162b2 and mRNA-1273 vaccines against SARS-CoV-2. *Albanian Journal of Trauma and Emergency Surgery*2021;5:791–6.
13 Benest J, Rhodes S, Quaife M, *et al*. Optimising vaccine dose in inoculation against SARS-CoV-2, a multi-factor optimisation modelling study to maximise vaccine safety and efficacy. *Vaccines* 2021;9:78.
14 Logunov DY, Dolzhikova IV, Shcheblyakov DV, *et al*. Safety and efficacy of an rad26 and RAD5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia. *Lancet* 2021;397:671–81.
15 Ella R, Reddy S, Jogdand H, *et al*. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: interim results from a double-blind, randomised, multicentre, phase 2 trial, and 3-month follow-up of a double-blind, randomised phase 1 trial. *Lancet Infect Dis* 2021;21:950–61.
16 Ebinger JE, Fert-Bober J, Printsev I, *et al*. Prior COVID-19 infection and antibody response to single versus double dose mRNA SARS-CoV-2 vaccination. *medRxiv* 2021. doi:10.1101/2021.02.23.2125223 0. [Epub ahead of print: 26 Feb 2021].
17 Radbruch A, Chang HD. A long-term perspective on immunity to COVID determining the duration of protective immunity to infection by SARS-CoV-2 is crucial for understanding and predicting the course of the COVID-19 pandemic. clinical studies now indicate that immunity will be long-lasting. *Nature* 2021;595:359–60.
18 Heath PT, Galiza EP, Baxter DN, *et al*. Safety and efficacy of NVX-CoV2373 Covid-19 vaccine. *N Engl J Med* 2021;385:1172–83.
19 Tanriover MD, Doğanay HL, Akova M, *et al*. Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in turkey. *Lancet* 2021;398:213–22.
20 Han B, Song Y, Li C, *et al*. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine (CoronaVac) in healthy children and adolescents: a double-blind, randomised, controlled, phase 1/2 clinical trial. *Lancet Infect Dis* 2021;21:1645–53.
21 Frenck RW, Klein NP, Kitchin N, *et al*. Safety, immunogenicity, and efficacy of the BNT162b2 Covid-19 vaccine in adolescents. *N Engl J Med Overseas Ed* 2021;385:239–50.
22 Ali K, Berman G, Zhou H, *et al*. Evaluation of mRNA-1273 SARS-CoV-2 vaccine in adolescents. *N Engl J Med* 2021;385:2241–51.
23 Baden LR, El Sahly HM, Essink B, *et al*. Phase 3 trial of mRNA-1273 during the Delta-Variant surge. *N Engl J Med* 2021;385:2485–7.
24 India study: the mutant strain delta is still highly infectious to vaccinated people (in Chinese). Available: https://news.ifeng.com/c/86ytoZHE1Ua [Accessed 11 Jun 2021].
25 More than 4,100 people in the United States are still hospitalized or die after vaccination expert: no surprise (in Chinese). Available: http://news.haiwainet.cn/n/2021/0628/c3541093-32143827.html [Accessed 28 Jun 2021].
26 Duarte-Salles T, Prieto-Alhambra D. Heterologous vaccine regimens against COVID-19. *Lancet* 2021;398:94–5.
27 Borobia AM, Carcas AJ, Pérez-Olmeda M, *et al*. Immunogenicity and reactogenicity of BNT162b2 booster in ChAdOx1-S-primed participants (CombiVacS): a multicentre, open-label, randomised, controlled, phase 2 trial. *Lancet* 2021;398:121–30.
28 Germany recommends a mixed vaccination programme multiple studies have shown the effectiveness of real-world vaccines (in Chinese). Available: https://finance.sina.com.cn/world/2021-07-03/doc-ikqcfnca4749560.shtml [Accessed 3 Jul 2021].
29 Jara A, Undurraga EA, González C, *et al*. Effectiveness of an inactivated SARS-CoV-2 vaccine in Chile. *N Engl J Med* 2021;385:875–84.
30 Goldshtein I, Nevo D, Steinberg DM, *et al*. Association between BNT162b2 vaccination and incidence of SARS-CoV-2 infection in pregnant women. *JAMA* 2021;326:728–35.
31 Bergwerk M, Gonen T, Lustig Y, *et al*. Covid-19 breakthrough infections in vaccinated health care workers. *N Engl J Med* 2021;385:1474–84.
32 A total of 47 new infected people were reported in 10 days. this round of epidemic in Guangdong was caused by the mutated virus and spread very fast. China CDC brings a good news (in Chinese). Available: https://www.163.com/dy/article/GBB3DO5L0512B07B.html [Accessed 31 May 2021].
33 Wang Y, Chen R, Hu F, *et al*. Transmission, viral kinetics and clinical characteristics of the emergent SARS-CoV-2 delta VOC in Guangzhou, China. *EClinicalMedicine* 2021;40:101129.
34 The US CDC: COVID-19 delta strain can spread nine, or need to comprehensively change the anti-epidemic strategy (in Chinese). Available: https://world.huanqiu.com/article/44A55QTDmf4 [Accessed 31 Jul 2021].
35 Zhang Wenhong: the clinical data of COVID-1 mutant strain suggest that humans can still WIN this protracted war (in Chinese). Available: https://finance.sina.com.cn/jjxw/2021-06-13/doc-ikqcfnca0742676.shtml [Accessed 13 Jun 2021].
36 Novavax released Phase III clinical data for the vaccine with 90% efficacy (in Chinese). Available: https://finance.sina.com.cn/tech/2021-06-14/doc-ikqcfnca1018200.shtml [Accessed 14 Jun2021].
37 Choi A, Koch M, Wu K, *et al*. Serum neutralizing activity of mRNA-1273 against SARS-CoV-2 variants. *J Virol* 2021;95:e01313–21.
38 Large study: three vaccines used in Canada are extremely effective for worrying virus variants (in Chinese). Available: https://polarzone.se/Large study: Canada approved vaccines for worrying diseases (in Chinese) [Accessed 7 Jul 2021].
39 Wang F, An Z, Rodewald L, *et al*. Guangdong's study of the effectiveness of China's inactivated vaccines against the SARS-CoV-2 B.1.617.2 (delta) variant. *China CDC Wkly* 2021;3:728–30.
40 Emary KRW, Golubchik T, Aley PK, *et al*. Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7): an exploratory analysis of a randomised controlled trial. *Lancet* 2021;397:1351–62.
41 Lopez Bernal J, Andrews N, Gower C, *et al*. Effectiveness of Covid-19 vaccines against the B.1.617.2 (delta) variant. *N Engl J Med* 2021;385:585–94.

42 British Vaccine Research: Delta is too fierce that "herd immunity" becomes difficult. Available: https://www.sohu.com/a/484389831_267106 [Accessed 19 Aug 2021].
43 Sheikh A, Robertson C, Taylor B. BNT162b2 and ChAdOx1 nCoV-19 vaccine effectiveness against death from the delta variant. *N Engl J Med* 2021;385:2195–7.
44 Collie S, Champion J, Moultrie H, *et al*. Effectiveness of BNT162b2 vaccine against omicron variant in South Africa. *N Engl J Med* 2022;386:494–6.
45 Evans JP, Zeng C, Carlin C, *et al*. Neutralizing antibody responses elicited by SARS-CoV-2 mRNA vaccination wane over time and are boosted by breakthrough infection. *Sci Transl Med* 2022;14:eabn8057.
46 Delta challenge upgrade: UK confirmed cases increase 46% per week and the variation continues (in Chinese). Available: https://new.qq.com/omn/20210630/20210630A08QV300.html [Accessed 30 Jun 2021].
47 Israel Ministry of Health: Pfizer vaccine effectiveness against novel coronavirus variant strain Delta has decreased by 30% to 64% (in Chinese). Available: https://www.sohu.com/a/475778231_656058 [Accessed 6 Jul 2021].
48 Israel: delta strain reduces Pfizer vaccine (in Chinese). Available: https://finance.sina.com.cn/tech/2021-07-24/doc-ikqciyzk7280536.shtml [Accessed 24 Jul 2021].
49 Wang R, Zhang Q, Ge J, *et al*. Analysis of SARS-CoV-2 variant mutations reveals neutralization escape mechanisms and the ability to use ACE2 receptors from additional species. *Immunity* 2021;54:1611–21.
50 Zhou R, To KK-W, Peng Q, *et al*. Vaccine-breakthrough infection by the SARS-CoV-2 omicron variant elicits broadly cross-reactive immune responses. *Clin Transl Med* 2022;12:e720.
51 Who warns: the delta variant may increase infection exponentially (in Chinese). Available: http://www.chinanews.com/gj/2021/06-29/9509459.shtml [Accessed 29 Jun 2021].
52 British scientists: there will almost certainly be a novel coronavirus variant that weakens the existing vaccine (in Chinese). Available: https://mil.news.sina.com.cn/2021-08-03/doc-ikqciyzk9194487.shtml [Accessed 3 Aug 2021].
53 Elliott P, Haw D, Wang H. REACT-1 round 13 final report: exponential growth, high prevalence of SARS-CoV-2 and vaccine effectiveness associated with delta variant in England during may to July 2021. Available: http://hdl.handle.net/10044/1/90800 [Accessed 4 Aug 2021].
54 Pfizer acknowledged that its immunity weakened six months after vaccination and was developing a third pin enhancer (in Chinese). Available: https://www.sohu.com/a/476401438_120388781 [Accessed 9 Jul 2021].
55 Moderna reports second quarter fiscal year 2021 financial results and provides business updates. Available: https://investors.modernatx.com/static-files/c43de312-8273-4394-9a58-a7fc7d5ed098 [Accessed 5 Aug 2021].
56 Pan H, Wu Q, Zeng G. Immunogenicity and safety of a third dose, and immune persistence of CoronaVac vaccine in healthy adults aged 18-59 years: interim results from a double-blind, randomized, placebo-controlled phase 2 clinical trial. *medRxiv* 2022.
57 Choi A, Koch M, Wu K, *et al*. Safety and immunogenicity of SARS-CoV-2 variant mRNA vaccine boosters in healthy adults: an interim analysis. *Nat Med* 2021;27:2025–31.
58 Singanayagam A, Hakki S, Dunning J, *et al*. Community transmission and viral load kinetics of the SARS-CoV-2 delta (B.1.617.2) variant in vaccinated and unvaccinated individuals in the UK: a prospective, longitudinal, cohort study. *Lancet Infect Dis* 2022;22:183–95.
59 Ai J, Zhang H, Zhang Y, *et al*. Omicron variant showed lower neutralizing sensitivity than other SARS-CoV-2 variants to immune sera elicited by vaccines after boost. *Emerg Microbes Infect* 2022;11:337–43.
60 Nemet I, Kliker L, Lustig Y, *et al*. Third BNT162b2 vaccination neutralization of SARS-CoV-2 omicron infection. *N Engl J Med* 2022;386:492–4.
61 Accorsi EK, Britton A, Fleming-Dutra KE, *et al*. Association between 3 doses of mRNA COVID-19 vaccine and symptomatic infection caused by the SARS-CoV-2 omicron and delta variants. *JAMA* 2022;327:639–51.
62 Regev-Yochay G, Gonen T, Gilboa M, *et al*. Efficacy of a fourth dose of Covid-19 mRNA vaccine against omicron. *N Engl J Med* 2022;386:1377-1380.
63 High viral load, rapid progression delta virus changes the definition of contact (in Chinese). Available: https://www.sohu.com/a/474606032_362042 [Accessed 29 Jun 2021].
64 Zhang Z, Li X, Wang Q, *et al*. Field Simulation of Aerosol Transmission of SARS-CoV-2 in a Special Building Layout - Guangdong Province, China, 2021. *China CDC Wkly* 2021;3:711–5.
65 Breakthrough infection after vaccination: delta strain is three times other (in Chinese). Available: https://finance.sina.com.cn/tech/2021-08-19/doc-ikqciyzm2384255.shtml [Accessed 19 Aug 2021].
66 Omicron affected 28 provinces Why is the proportion of asymptomatic infected persons increasing?(in Chinese). Available: https://www.163.com/dy/article/H2H53LCG0512D3VJ.html [Accessed 15 Mar 2022].
67 The US version of the health code is embarrassed: maximize privacy protection epidemic tracking is basically ineffective (in Chinese). Available: https://finance.sina.com.cn/stock/relnews/us/2020-12-15/doc-iiznezxs6993052.shtml [Accessed 15 Dec 2020].
68 A 2-year-old boy in Nanjing was infected by nucleic acid tests many nucleic acid detection personnel dense disorder (in Chinese). Available: https://3g.163.com/dy/article_cambrian/GGQ5U9V1052583KJ.html [Accessed 7 Aug 2021].
69 From Nanjing to Zhangjiajie, why did the epidemic transmission chain lose layers? (in Chinese). Available: http://www.chinanews.com/gn/2021/07-29/9531239.shtml [Accessed 29 Jul 2021].
70 The French Prime Minister's "health code" was exposed and his personal information was leaked The Prime Minister's office responded(in Chinese). Available: https://www.163.com/dy/article/GKDUEBTA0514R9L4.html [Accessed 21 Sept 2021].
71 Yaga D, Mell P, Roby N. Blockchain technology overview, 2018. Available: https://doi.org/10.6028/NIST.IR.8202 [Accessed 9 Sept 2021].
72 Gao S, Lu Y, Wang S. The application of Blockchain technology in Whole-process vaccine traceability system (in Chinese). *Chin J Health Info Manag* 2019;16.
73 Shao C. Vaccine tracing framework based on blockchain technology (in Chinese). *China Medical Engineering* 2021;29:37–9.
74 Kalla A, Hewa T, Mishra RA, *et al*. The role of Blockchain to fight against COVID-19. *IEEE Engineering Management Review* 2020;48:85–96.
75 Qiu Z, Zhu Y. A novel structure of Blockchain applied in vaccine quality control: double-chain structured Blockchain system for vaccine Anticounterfeiting and traceability. *J Healthc Eng* 2021;2021:6660102.
76 What role has blockchain played in the fight against COVID-19? What progress has been made in the application of blockchain in the post-epidemic era?(in Chinese). Available: https://www.bitcoin86.com/block/75079.html [Accessed 29 Nov 2021].
77 Wang T, Zhao Y. Prevention, control and evaluation of COVID-19 epidemic based on Health-code Blockchain (in Chinese). *Acta Mathematicae Applicatae Sinica* 2020;43.
78 Zhang Y, Peng Y, Li W. Analysis of asymptomatic COVID-19 infections and conversion to diagnose in Sichuan Province (in Chinese). *J Prev Med Inf*2021;37.
79 Yu S, Di C, Chen S, *et al*. Distinct immune signatures discriminate between asymptomatic and presymptomatic SARS-CoV-2^{pos} subjects. *Cell Res* 2021;31:1148–62.
80 Sun T, Cui J. Modeling the asymptomatic infections for COVID-19 epidemic in China (in Chinese). *Acta Scientiarum Naturalium Universitatis Sunyatsenz* 2021;60:103–10.
81 Al-Sadeq DW, Nasrallah GK. The incidence of the novel coronavirus SARS-CoV-2 among asymptomatic patients: a systematic review. *Int J Infect Dis* 2020;98:372–80.
82 Li Z, Lin J, Pu R. Asymptomatic transmission in the COVID-19 pandemic: a systematic review and meta-analysis (in Chinese). *Chin J Dis Control Prev* 2021;25:445–53.
83 Li M, Yuan H, Cao Y. Analysis of infectivity of asymptomatic carriers of COVID-19 in Sichuan Province (in Chinese). *Prev Med Inf* 2021;37.
84 Mahajan A, Solanki R, Sivadas N. Estimation of undetected symptomatic and asymptomatic cases of COVID-19 infection and prediction of its spread in the USA. *J Med Virol* 2021;93:3202–10.
85 Irons NJ, Raftery AE. Estimating SARS-CoV-2 infections from deaths, confirmed cases, tests, and random surveys. *Proc Natl Acad Sci U S A* 2021;118:e2103272118.
86 Pei S, Yamana TK, Kandula S, *et al*. Burden and characteristics of COVID-19 in the United States during 2020. *Nature* 2021;598:338–41.
87 Ye J. Analysis on Measures and Enlightenment of South Korea's Epidemic Response to COVID-19. In: *Global science, technology and economy outlook*. , 2020: 35, 60–8.
88 Vuong Q-H, Le T-T, La V-P, *et al*. Covid-19 vaccines production and societal immunization under the serendipity-mindsponge-3D knowledge management theory and conceptual framework. *Humanit Soc Sci Commun* 2022;9:22.

89 Roberts GHL, Partha R, Rhead B, *et al*. Expanded COVID-19 phenotype definitions reveal distinct patterns of genetic association and protective effects. *Nat Genet* 2022;54:374–81.

90 Markov PV, Katzourakis A, Stilianakis NI. Antigenic evolution will lead to new SARS-CoV-2 variants with unpredictable severity. *Nat Rev Microbiol* 2022;20:251–2.