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Sheet, Surveillance, Strategy, Salvage and Shield in global biodefense system to protect the public health and tackle the incoming pandemics

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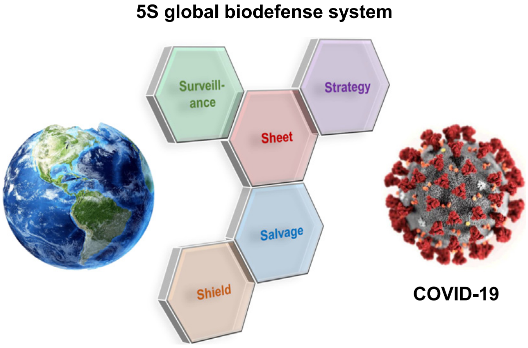
HIGHLIGHTS

- Sheet, Surveillance, Strategy, Salvage and Shield are key components of global biodefense system.
- Each component in 5S system uniquely contributes to the prevention and control of COVID-19 and other emerging infectious diseases.
- 5S global biodefense system requires international collaboration and integral application.

GRAPHICAL ABSTRACT



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ABSTRACT

The pandemic of COVID-19 challenges the global health system and raises our concerns on the next waves of other emerging infectious diseases. Considering the lessons from the failure of world's pandemic warning system against COVID-19, many scientists and politicians have mentioned different strategies to improve global biodefense system, among which Sheet, Surveillance, Strategy, Salvage and Shield (5S) are frequently discussed. Nevertheless, the current focus is mainly on the optimization and management of individual strategy, and there are limited attempts to combine the five strategies as an integral global biodefense system. *Sheet* represents the biosafety datasheet for biohazards in natural environment and human society, which helps our deeper understanding on the geographical pattern, transmission routes and infection mechanism of pathogens. Online surveillance and prognostication network is an environmental *Surveillance* tool for monitoring the outbreak of pandemic diseases and alarming the risks to take emergency actions, targeting aerosols, waters, soils and animals. *Strategy* is policies and legislations for social distancing, lockdown and personal protective equipment to block the spread of infectious diseases in communities. Clinical measures are *Salvage* on patients by innovating appropriate medicines and therapies. The ultimate defensive *Shield* is vaccine development to protect healthy crowds from infection. Fighting against COVID-19 and other emerging infectious diseases is a long rocky journey, requiring the common endeavors of scientists and politicians from all countries around the world. 5S in global biodefense system bring a ray of light to the current darkest and future road from environmental and geographical perspectives.

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Contents

1. Introduction

The outbreak of coronavirus infectious disease-2019 (COVID-19) pandemic has rapidly spread throughout over 200 countries, posing a global threat to human health. World Health Organization (WHO) declared a Public Health Emergency of International Concern on 10th March, 2020. Till 10th April 2021, there are 130 million confirmed cases and 2.9 million deaths (WHO, 2021). SARS-CoV-2 is an enveloped, positively-stranded RNA virus belonging to the beta coronavirus genus that causes COVID-19 (Lai et al., 2020). It can transmit among people (Chan et al., 2020; Chang et al., 2020; Li et al., 2020b; Poon and Peiris, 2020) *via* direct contact, respiratory droplet routes (Carlos et al., 2020; Lai et al., 2020; Wu et al., 2020a) and potentially fecal or aerosol (Lai et al., 2020). The COVID-19 pandemic challenges the global health system and raises our concerns on the next waves of other emerging infectious diseases. Considering the lessons from the failure of world's pandemic warning system against COVID-19 (Balboa et al., 2021), it is of great urgency to think about why we fail to fight against the COVID-19 and what we should prepare for tackling the future emerging infectious diseases for global public health.

Some countries have achieved effective regional control of the COVID-19 epidemic; however, there are four successive waves globally, including January 2020 to April 2020 in China, April 2020 to June 2020 in Europe, October 2020 to March 2021 in USA and Europe, and March 2021 to June 2021 in India. This disappointed situation so far is attributing to our limited knowledge about SARS-CoV-2 and lack of effective medicines and vaccines to stop this pandemic. In addition, strategies tackling this public health emergency still lack experience in social distancing and personal protection, and the current surveillance tools cannot meet the requirement for clinical and environmental diagnosis for effective prevention and control. Although some countries are trying to survive this epidemic through natural herd immunity, it is questionable and criticized (Lindström, 2020). As a global pandemic, any simple strategy might not work efficiently (Forman et al., 2021). Accordingly, the concept of global biodefense system is raised as an extremely vulnerable approach to fight against the COVID-19 and incoming pandemics (Forman et al., 2020), which needs the cooperation of all countries around the world to overcome the above-mentioned urgent problems.

Considering the critical challenges and lessons from the failure in tackling the COVID-19, the global biodefense system should consist of multiple strategies for not only this COVID-19 pandemic but also future public health emergencies. This study critically reviews the recent progresses and strategies in fighting against the COVID-19 pandemic from geographic aspects, and unravel the five key components in the global biodefense system as 5S of *Sheet*, *Surveillance*, *Strategy*, *Salvage* and *Shield*. We comprehensively discuss the roles and limitations of each strategy, characterize their advantages and feasible scenarios, properly integrate the five strategies for effective prevention and control of the pandemics, and offer suggestions for establishing the 5S global biodefense system to tackle the COVID-19 and other emerging infectious diseases.

2. Sheets: database for biohazards in natural environment and human society to help deeper understanding on the geographical patterns, transmission routes and infection mechanisms of pathogens

Sheet strategy refers to the establishment and management of pathogen databases to better understand their features of geographical patterns, transmission routes and infection mechanisms. Many bacterial strains and viruses have been identified as pathogens possessing significant threats to human health and public security. Pathogenic bacteria are a group of single-celled microorganisms widely distributed in environmental media or symbiotic with other organisms (Fredrickson et al., 2004). In contrast, viruses have no cell structure and cannot survive independently (Brown and Bhella, 2016). They can only parasitize and reproduce in living cells, exhibiting the characteristics of high hereditary variability (Hermans et al., 2017). Pathogens can transmit in numerous ways, both horizontally (*e.g.*, through the respiratory tract, digestive tract, genitourinary tract, skin wounds and blood) and vertically (*e.g.*, from mother to baby through the placenta, birth canal and breastfeeding) (Lipsitch et al., 1996). As each pathogenic strains or viruses have unique transmission routes and infectious features, it is critical to understand their physiological properties for effective prevention and control (Zhang et al., 2022). *Escherichia coli* has a short generation cycle of about 20 min and can rapidly duplicate in ambient environment, transmitting through food, water or close contact and causing gastrointestinal tract infection or urethra of humans and many animals (Kaper et al., 2004). Intestinal pathogenic poliovirus spreads rapidly after entering the human body and begins replication within a few hours, mainly following the fecal-oral transmission (Tang et al., 1989). As its contagiousness can last for 2 months after excretion in feces, people with low immunity are extremely vulnerable to poliovirus in environmental media (Tang et al., 1989). By establishing pathogen databases, it allows global scientific researchers to access to their resources, trace origins, automate the comparison of their genetic information, and find potential answers for subsequent clinical trials (Pickett et al., 2012).

Since the SARS pandemic in 2003, scientists have been continuously working on pathogen databases. The Virus Pathogen Database and Analysis Resource (ViPR) is a successful case, which provides a platform for performing complex analysis workflows, generating experimentally verifiable hypotheses and sharing data with collaborators (Pickett et al., 2012). Some databases for specific pathogens have also been established for HIV (Kuiken et al., 2003), euHCVdb (Combet et al., 2007), HFV/Ebola (Kuiken et al., 2012) and influenza (Bao et al., 2008) (Table 1). For instance, hepatitis D virus (HDV) is listed as Group 3 carcinogenic agents (not classifiable as to its carcinogenicity to humans) by International Agency for Research on Cancer (IARC), and HDVdb database provides integrated general or specialized sequence analysis tools and enables the investigation on the genetic variation of all available HDV sequences, the correlation of genotypes with epidemiology and pathogenesis, and the drug-resistant mutations for development of effective vaccines (Usman et al., 2020). Facing the threats of COVID-19, the China National Bioinformatics Center (CNBC) and the National Genome Science Data Center

Table 1
Established databases (*Sheet*) for pathogens.

Database name	Target pathogens	Authorities	Link	Reference
HDVdb	Hepatitis D virus (HDV)	Department of Bioinformatics, Wissenschaftszentrum Weihenstephan, Technische Universität München; Institute of Virology, Technische Universität München; Division of Clinical Pharmacology, University Hospital, LMU Munich	http://hdvdb.bio.wzw.tum.de	(Usman et al., 2020)
2019 Novel Coronavirus Information Database	SARS-CoV-2	China National Bioinformatics Center (CNBC) and the National Genome Science Data Center (NGDC)	https://bigd.big.ac.cn/ncov	(Wang et al., 2019)
HIV Sequence Databases	HIV	Los Alamos; Stanford	http://www.hiv.lanl.gov/ http://hivdb.stanford.edu	(Kuiken et al., 2003)
European hepatitis C virus database	euHCVdb	CNRS and Univeresity of Lyon	https://euhcvdb.ibcp.fr/euHCVdb/	(Combet et al., 2007)
HFV sequence, immunological data	HFV/Ebola DB	LANL	http://hfv.lanl.gov	(Kuiken et al., 2012)
Influenza sequence database	Influenza virus	NCBI	http://www.ncbi.nlm.nih.gov/genomes/FLU	(Bao et al., 2008)

(NGDC) jointly established the 2019 Novel Coronavirus Information Database (https://bigd.big.ac.cn/ncov) to promote the data sharing of SARS-CoV-2 genetic information and allow timely access to the database by the global public (Zhao et al., 2020). CNBC and NGDC collect and publish nucleotides and proteins, academic papers and news about SARS-CoV-2, servicing for the analysis of coronavirus genome sequence variation and providing convenient data support for global academia to carry out in-depth research on SARS-CoV-2. Considering the global consequences of the COVID-19 and other pandemics, our understanding of the mechanisms of pathogen evolution in natural hosts, migration in environmental medium, and infection in new hosts needs improvement (Prussin et al., 2018). For instance, it is critical to know how far and fast droplets spread for transmission risk assessment, and data about the evaporation and deposition of droplets released during respiration and the size distribution and viral load of viruses need to be investigated and shared in database for appropriate decision making on the social distance and lockdown strategy (de Oliveira et al., 2021).

Databases about pathogens in natural environment are also critical in *Sheet* strategy. Most of pathogens have been identified in natural hosts, and some severe zoonoses originate from wild hosts (Morse et al., 2012), *e.g.*, the Middle East Respiratory Syndrome (MERS), Zika virus, avian influenza, and brucellosis. SARS-CoV has been confirmed to originate from wild bats (Menachery et al., 2015), and SARS-CoV-2 is also highly hypothetically from wild animals (Ye et al., 2020). Since the wild hosts have their unique habitats or live in specific biological communities, natural focal diseases only exist in limited regions with obvious geographic distribution patterns (Tang, 2005). In addition, pathogen transmission is not limited to person-to-person or person-to-animal pathway, but also in natural and environmental quasi-hosts (Li et al., 2020a). Social environment is also a potential medium of viral transmission and poses a great threat to human health (Ong et al., 2020), as the presence of SARS-CoV-2 in samples of the COVID-19 patients' surrounding air and high-contact surfaces is proven to relate to the onset days of the patients (Chia et al., 2020). Pathogens might cross the ecological barrier and spill over into surrounding environment or other animals (Zhang et al., 2021a), causing potential spread in human societies by invasion of wildlife habitats and consumption of wild animals. For instance, mosquitoes are key intermediate hosts of many infectious diseases and the outbreak of dengue fever is highly associated with the active regions of mosquitoes in tropical Africa (Gubler, 1998). In addition, 8 out of 11 first reported infectious cases of Ebola diseases are reported to occur in areas with high degree of forest destruction, explained by the invasion of humans in the habitats of wild bats carrying Ebola viruses (Rulli et al., 2017). Therefore, in-depth geographic study of these pathogens is of great significance for preventing and controlling the occurrence of natural foci-borne diseases. Understanding pathogenic geographic distribution can help us identify hot spots, carry out targeted epidemic prevention and control actions, and prevent their spillover (Pérez-Trallero et al., 2005).

Besides the physiological features and natural occurrence of pathogens, *Sheet* strategy should also cover the models of viral transmission and spread among social communities (Brockmann and Helbing, 2013). Exponential growth model is usually used to predict and forecast viral transmission and infectious cases; however, it only works during early virus onset when the public is not aware of the disease (Viboud et al., 2016). Thus, geography-assisted modelling is key to improve prediction accuracy. A Moving Average method is effective for forecasting short-range COVID-19 cumulative cases in 1–7 days at the county, health district, and state levels in USA (Lynch and Gore, 2021). Another spatial lag model predicts factors related to the increasing risks of COVID-19 in Brazil, including spatial effects, distortions and Gini index, considered as an effective guide for interventions and control of the COVID-19 (Weststrate et al., 2019). In addition, by comprehensively considering viral physiological information in database, sociological indicators, and public activity characteristics, complex network methods are used to establish a global influenza transmission model to describe its worldwide dynamics (Li, 2019). This model can predict the origins, convergence points and spreading trends of influenza virus, benefiting different prevention and control strategies tackling influenza epidemics across countries to its global impacts.

In summary, *Sheet* strategy can initiate the fight against the emerging infectious diseases by establishing biohazardous databases in natural environment and human society to help our deeper understanding on the geographical patterns, transmission routes and infection mechanisms of pathogens. Well-established *Sheet* strategies can provide a consensus contribution to studies on global or reginal epidemiology and patient clinical data, by offering key facts from biological, geographic, environmental and social aspects, and derive recommendations to the surveillance, prognostication, prevention and control of the emerging infectious diseases (Ahmed et al., 2020). Governments around the world also have an obligation to build up the global pathogen *Sheet* and achieve the goals of collaboration on the prevention and control of zoonoses, for protecting biodiversity, addressing global environmental problems, and suppressing the illegal invasion of wildlife habitats (Córdoba-Aguilar et al., 2021). Particularly, *Sheet* strategy might help us in predicting the area of scenic spots for the bloom and spread of the emerging infectious diseases and taking timely and effective prevention and control measures in advance.

3. Surveillance: tools for the prevention and control of pandemic diseases by environment-based epidemiology

Many molecular tools have been developed to trace pathogens in environmental media, including quantitative polymerase chain reaction (qPCR), colloidal gold immunochromatography and traditional culture methods (TCM) (Clark et al., 1986; Heid et al., 1996; Shaw et al., 2013), similar as those used for clinical diagnosis to confirm patients. As many pathogens are present in environmental media, environmental-based epidemiology (EBE) is therefore raised as a good approach for the surveillance and prognostication of the emerging infectious diseases, including epidemiology of wastewater-based surveillance (WBE) and aerosol-based surveillance (ABE) (Table 2) (Ahmed et al., 2021; Ahmed et al., 2020; Arora

Table 2

Examples of environmental-based epidemiology (EBE) as *Surveillance* tools for monitoring and prognostication of SARS-CoV-2.

Environmental media	Location	Details	Performance	Reference
Wastewater	University of Arizona (USA)	650 wastewater samples from 24th August to 20th November, 2020	Successful establishment of a WBE-surveillance network, identification of infected people and effective prevention/control of the COVID-19 in campus	(Betancourt et al., 2021)
Wastewater	Wastewater treatment plants (Qatar)	43 samples from 21st June to 30th August 2020	Monitoring trends in the number of people infected in Qatar, more reliable than RT-qPCR diagnostic tests.	(Saththasivam et al., 2021)
Wastewater	Six major urban centers (UK)	Samples from six WWTPs between March and July 2020	Theoretical basis for epidemic control strategies to control the transmission of SARS-CoV-2.	(Hillary et al., 2021)
Wastewater	Bangladesh	16 samples between 10th July and 29th August 2020	Successful monitoring of SARS-COV-2 by replacing sewer system with urban main drainage system.	(Ahmed et al., 2021)
Wastewater	Southeastern Virginia (USA)	Weekly samples from nine WWTPs from mid-March into late July	Successful method to analyze and present WBE data to compare with clinical results.	(Gonzalez et al., 2020)
Wastewater	Australia	9 samples with a potential detection windows (28 days); between January and April 2020	Successfully identification of the infected persons at a median range of 171 to 1090 in the catchment. WBE has the potential to provide early warning signals about the extent of its spread in the community.	(Ahmed et al., 2020)
Wastewater	India	Samples were collected from 8 sites between 3rd May 2020 and 14th June 2020.	Successful population-level burden estimates for future outbreaks of SARS-COV-2.	(Arora et al., 2020)
Air & Surface	Beijing (China)	Exhaled breath samples had the highest positive rate (26.9%, $n = 52$), followed by surface swabs (5.4%, $n = 242$) and air samples (3.8%, $n = 26$)	Patients exhale a lot of aerosols, which can be used for indoor safety diagnosis in medical institutions.	(Ma et al., 2021)
Air & Surface	UK	Sampling of air close to 6 asymptomatic and symptomatic COVID-19 patients with and without surgical masks; 21 cases of frequent contact with environmental surfaces	A significant correlation between viral load range in clinical samples and positive rate in environmental samples ($p < 0.001$).	(Cheng et al., 2020)

et al., 2020; Betancourt et al., 2021; Cheng et al., 2020; Gonzalez et al., 2020; Hillary et al., 2021; Kuiken et al., 2012; Ma et al., 2021; Saththasivam et al., 2021). For instance, SARS-CoV-2 is frequently detected in wastewater (Zhang et al., 2020c) and aerosol (Chia et al., 2020) or on solid surface (Ong et al., 2020), and the significant spillover of SARS-CoV-2 in hospital outdoor environment raises the demands to keep SARS-CoV-2 under close surveillance (Zhang et al., 2021c). How to interrogate SARS-CoV-2 in environmental samples by EBE draws increasing attentions for effectively tracking the COVID-19 and asymptomatic patients. From geographic point of view, EBE can benefit the prevention and control of infectious diseases in terms of their source, evolution, transmission, spread, prevention and control (WHO, 2018).

WBE is first outlined in 2001 as a tool for evaluating the use of alcohol and illicit drugs and drug abuse treatment in the community (Daughton, 2001; Du et al., 2015; Rodriguez-Alvarez et al., 2015; van Nuijs et al., 2011; Zuccato et al., 2008). It is based on chemical analysis of contaminants and biomarkers in wastewater to obtain qualitative and quantitative data on the activities of people living in a particular wastewater catchment (Lorenzo and Picó, 2019). WBE can provide information on substance use and exposure to environmental chemicals (Lai et al., 2018; Lorenzo and Picó, 2019). Regarding the fact that wastewater contains biomarkers of lifestyle and health, WBE cab be also used to estimate the prevalence of certain diseases.

As infectious diseases are viewed as a critical threat to global public health today, WBE has been introduced as a new epidemiology tool for current infectious disease surveillance system by evaluating the emergence of new disease outbreak to social community in real-time, including acute childhood diarrhea (Kolahi et al., 2010), Hepatitis E (Guillois et al., 2016), human Sapoviruses (Kitajima et al., 2011), Czyptosporidium, Giardia, Cyclospora (Kitajima et al., 2014), human noroviruses (Kitajima et al., 2012; Sokolova et al., 2015) and other pathogenic viruses (Shrestha et al., 2018). Through the analysis of population pooled wastewater, WBE can map the spread of infectious diseases and offer clues for further advancement as an early warning system (Sims and Kasprzyk-Hordern, 2020).

Facing the unprecedented global public health crisis caused by the COVID-19, WBE has been given high expectations as a promising surveillance and prognostication tool for the administrative and social significance to control the epidemic (Siddique et al., 2021). WBE together with mathematical models can estimate the trends of COVID-19 and other emerging infectious diseases in the discharge area (Henderson, 1997). WBE in the University of Arizona (USA) successfully identified and isolated 3 infected people with the aid of clinical test, remarkably contributing to the design of a WBE-surveillance network in the fall semester and the prevention and control of the COVID-19 in campus (Betancourt et al., 2021). Another example of WBE on raw municipal wastewater from five wastewater treatment plants in Qatar successfully mirrored the number of new daily positive cases (Saththasivam et al., 2021). In addition, WBE can also evaluate the disease control measures by monitoring the prevalence of SARS-CoV-2 and other human pathogens in the population. From March to July 2020, a longitudinal analysis of SARS-CoV-2 in the sewage of 3 million residents in six major urban centers in the UK identified the genetic variations in wastewater and alarmed the spread of SARS-CoV-2 mutants in local community, providing information for the public health decision-making (Hillary et al., 2021). In Bangladesh, SARS-CoV-2 genetic materials were identified in wastewater and significantly accumulated in main ditches, hinting at the feasibility to survey SARS-CoV-2 in the main drainage system instead of wastewater pipelines for public health protection at city level (Ahmed et al., 2021). Evidence-based virus testing in wastewater not only facilitates centralized testing, but also provides a potential community for vaccine distribution. Therefore, governments can shorten the lockdown period, thereby alleviating human pressure and promoting economic growth (Panchal et al., 2021). Since China began to study WBE in 2011, WBE monitoring has successfully provided great support for screening the use of primary drugs and new psychoactive substances in major cities in China, recently achieving significant improvement for drug abuse management in Beijing and Shenzhen (Li et al., 2019). Besides WBE, ABE is also developed for the effective prevention and control of the COVID-19 pandemic, as the inhalation of pathogen-containing droplets is a recognized mode of transmission of many infectious diseases in humans and animals (Prussin et al., 2018). Aerosol viruses are most easily exposed to air and road surfaces, and exhaled viruses per hour are of several million in the early stage of the COVID-19 patients (Ma et al., 2021). As exhaled aerosols are reported to be the most likely culprits of SARS-CoV-2 transmission, it is therefore attractive to track SARS-CoV-2 in aerosols (Chia et al., 2020; Ong et al., 2020) and use ABE for effective monitoring in medical institutions to determine viral load and alarm SARS-CoV-2 spread (Miller et al., 2021). ABE also provides insight into the likely direction of viral transmission and the effectiveness of protective measures, helping in decision making for preventive measures on public transport to reduce the transmission risks of SARS-CoV-2 viruses.

Despite the significant advantages in tracking COVID-19 patients and prognostication, WBE currently faces some critical challenges. Firstly, all WBE studies require manual sample collection, and there is still lack of automatic and rapid sampling devices assisting WBE. Manually sample collection is laborious and time-consumption, normally requiring several well-protected staffs for sample handling and transferring. These limitations restrict the simultaneous surveillance of SARS-CoV-2 in real time, which is essential to control the spread at the early stage of an outbreak (Rallapalli et al., 2021), and challenge the applicable scenario with prolonged detection duration and poor time-efficiency, leaving limited, rare or underreported data for public health agencies to extrapolate the main route of transmission from large-scale population epidemic data (Atkins et al., 2015). Therefore, some low-cost autosampling devices have been developed to achieve high-resolution monitoring of SARS-CoV-2 in wastewater at smaller scales with an acceptable frequency (Reeves et al., 2021; Schang et al., 2021), allowing the coverage of the dense surveillance network at a scale of city or country. In addition, a rapid SARS-CoV-2 interrogation is suggested for WBE and ABE in tracking COVID-19 patients by online surveillance and prognostication network (Udugama et al., 2020). This network can monitor the dynamics of SARS-CoV-2 in wastewater or aerosols for COVID-19 or asymptomatic patients in the monitored areas. Together with contact-tracing apps, the public are aware of whether they have overlapped trajectory with the suspicious high-risk areas and then take appropriate actions. Secondly, the most diagnostic method used for WBE or ABE is RT-qPCR, which requires laborious pretreatment and a thermo cycler (Udugama et al., 2020). It brings difficulties in the design and manufacture of auto-samplers and -detectors. New methods with the on-site detection potential shine lights on EBE, *e.g.*, loop mediated isothermal amplification (LAMP) (Tomita et al., 2008), field-effect transistor (FET) (Park et al., 2014) and Surface-enhanced Raman spectroscopy (SERS) (Zhang et al., 2021b). Thirdly, the algorithms and mathematical models in WBE to track COVID-19 cases remain a daunting challenge and need further study (Zhu et al., 2021). To quickly identify infected individuals or communities, the sampling strategy-target positioning, time and interval targets need to be optimized to suit the purpose and scope of WBE (Bandala et al., 2021). Recently, a new target group identification and location optimization method is proposed for the maximum probability detection of SARS-CoV-2 wastewater network by the fuzzy Bayesian model to reduce the uncertainty of data and help in decision making (Rallapalli et al., 2021).

4. Strategy: policies and legislations for personal protection, social distancing, lockdown and trace-track to block the spread of infectious diseases in communities

From the long history fighting against infectious diseases, many policies and regulations have focused on social network and behavior to mitigate transmission risks. Public social distancing can increase the outbreak threshold of an infectious disease, and thus is considered as an effective control strategy to reduce infection risks (Huang et al., 2021b). The public health interventions of geographically targeted prophylaxis and social distancing are reported to halt the pandemic caused by highly pathogenic H5N1 influenza A viruses in early stages (Ferguson et al., 2005). Particularly during the H1N1 epidemic, symptomatic persons with appropriate social distancing sufficiently reduce their social contact and decrease the reproduction number to about one-quarter, comparing to those who have normal social activities and cause a faster transmission (Van Kerckhove et al., 2013).

Based on the experiences and lessons from the SARS pandemic in 2003, China acts quickly to avoid the recurrence of the tragedy and has been committed to seeking more effective physical interventions to block or reduce the viral transmission of SARS-CoV-2 in the initial stage of the COVID-19 (January 2020). Since the outbreak of the COVID-19 epidemic, countries around the world have taken different policies and legislations for personal protection, social distancing, lockdown and trace-track to block the spread of the COVID-19 in communities. Among the adopted strict measures, the main ones include compulsory isolation, blockade, extensive screening and nucleic acid testing on returnees from overseas and migrants in high-risk areas (Murphy, 2020). In addition, China has obtained new experience to further deploy epidemic prevention and control work. China Health Commission publicly reports daily statistics on new cases and release the strategic information in a timely and transparent manner, and serious accountability is taken for delayed, concealed, and under-reported cases (Liu et al., 2020). China also takes the initiative to respond to social concerns, promote epidemic prevention knowledge, and strengthen cooperation with WHO and other countries. Accordingly, the COVID-19 epidemic is well controlled within China, and there are only occasional cases associated with immigration or international cold chain logistics (Chen et al., 2021).

In response to the COVID-19 epidemic, many countries have adopted various levels of physical intervention, mainly including entry and exit screening, isolation, quarantine, blockade, social distancing, personal protection, *etc.* (Jefferson et al., 2020). Nevertheless, not many countries have successfully controlled the epidemic like China due to factors such as national structure, culture, policies, demographic characteristics, citizen trust and technical administration (Baniamin et al., 2020). Some countries like the United States, Britain and Italy cannot take experience from China and implement many measures for their inherently free and democratic politics. The Netherlands and Sweden only encourage residents to maintain social distancing without any blockade actions, attempting to adopt a policy of inaction to achieve herd immunity while maintaining economy (Frey, 2020). However, the fact is that the epidemic is developing in an uncontrollable direction, and these countries have to take remedial measures. Countries with better performance (Germany, Singapore, *etc.*) initiate extensive testing for SARS-CoV-2 since the first domestic case, and implement a policy of quarantine on confirmed and suspected cases, thereby suppressing the spread of the COVID-19 cases (Beaubien, 2020). Other countries like Israel and South Korea introduce more advanced artificial intelligence technology and big data analysis to assist in the prevention and control of the COVID-19 epidemic under the premise of implementing various policies, and have also obtained more significant effects (Holmes, 2020; Islam, 2020).

Both experiences and lessons in the last 20 months fighting against the COVID-19 give us clues how to effectively prevent and control the COVID-19 and other emerging infectious diseases, and the key strategies include personal protection, social distancing, lockdown and trace-tracking.

Common personal protection measures include: (1) wash hands frequently; (2) no touch on eyes, nose and mouth with hands; (3) wear masks, goggles and protective gloves; (3) sneeze into elbows; (4) wipe the surfaces that touch objects with alcohol; (5) keep a social distance of more than 1 m from others (Jefferson et al., 2020). Among them, wearing protective masks is the most effective measure to prevent respiratory infections, followed by hand hygiene management (Chaabna et al., 2021). The strict regulations in China to wear masks in public area including hospitals, transport vehicles, restaurants, cinemas, supermarkets and other crowded places remarkably contribute to the successful control of the COVID-19, giving valuable suggestions for other countries. In addition, regarding the potential spillover of SARS-CoV-2 from hospitals and feces (Zhang et al., 2021c), contaminated discharge and sites must be compulsorily and completely disinfected under the guidance of disease prevention and control agencies or in accordance with sanitary requirements (Liu et al., 2020). Personal protection devices should also be further upgraded to have better effectiveness, environmental friendliness and long-life (Rodríguez et al., 2021).

Based on extensive studies of respiratory transmitted viruses such as SARS-CoV-2, SARS-CoV, and MERS, Chu et al. concluded that the likelihood of contacting coronavirus decreases with increasing social distance, and the best physical distance is two meters, at least no less than 1 m (Chu et al., 2020). Another study with time series analysis establishes an epidemiological remote monitoring model of population movement and investigates the correlation between social distance and epidemiological trends in 28 European countries, reaching similar conclusions (Vokó and Pitter, 2020). By simulating different types of quarantine, people exposed to confirmed or suspected cases reduce at least 44% of cases and 31% of mortality rate after quarantine measures (Nussbaumer-Streit et al., 2020). A model simulation shows that measures such as isolating infected people and their relatives, closing schools, and encouraging people to work from home can significantly reduce the number of infections by 99.3% within 80 days in Singapore (Koo et al., 2020).

In addition to social distancing and quarantine, lockdown is a typical regional policy to control the spread of the COVID-19 and other emerging infectious diseases. The average number of contacts between people is reported to reduce by 81% during the lockdown, largely avoiding physical contacts outside the home and effectively cutting off viral spread (Di Domenico et al., 2020). Wuhan (China) implements a city-wide lockdown at the first time on 23rd January 2020 and the doubling time of cases after the lockdown increased from 2 days to 4 days, suggesting the significant contribution of strict population lockdowns in high-risk areas to slow the spread of the COVID-19 (Lau et al., 2020). In mid-March 2020, many cities or even countries around the world, including New York City where the confirmed cases of the COVID-19 accounted for half cases in the United States, three-weeks national lockdown in the United Kingdom prohibiting multi-person gatherings, 21-day national lockdown in South Africa, and 21-day national blockade in India (Hamzelou, 2020). Lockdown has the advantage of alleviating socio-economic pressures and avoiding overrunning the health care system (Di Domenico et al., 2020). The best lockdown strategy is suggested to implement strict actions 2 weeks after the outbreak, covering 60% of the population 1 month later and evacuating gradually afterwards, which can maximize cost savings and yield the highest revenue (Alvarez et al., 2020).

Trace-tracking is another traditional disease control strategy. An Internet of Things (IoT) automatic tracking and tracing method in India is used by deploying cost-effective RFID tags and ACTS to identify possible contacts *via* personal mobile devices, enabling to identify and monitor the primary/secondary contacts by the administrative agencies and allowing in-time actions to prevent the social spread (Rajasekar, 2021). Trace-tracking strategy together with entry screening can effectively prevent the importation of the COVID-19 cases (Mouchtouri et al., 2020), as suggested by WHO to identify international travelers with symptoms and signs of viral infection or a history of viral exposure (WHO, 2014). In the early stage of the epidemic, the implementation of trace-tracking and entry screening is critical in effectively controlling the large-scale outbreak, as well as saving resources and costs, to prevent international spread or imported cases in local communities (Chetty et al., 2020; Mouchtouri et al., 2020; WHO). However, there are ethical concerns about the abuse of power and the disclosure of personal information (Coghlan et al., 2020), and thus it is crucial for policymakers to protect the security of trace-tracking and personal information.

These public health strategies tackling the COVID-19 pandemic are reported with satisfactory performance. Beyond policy formulation, it is critical for the government to win the trust and support of the people and guarantee for the implementation of these strategies. On the premise of ensuring the personal information security, government should designate public health strategies that are in line with the local actual situation, so as to reassure the people and voluntarily comply with relevant regulations.

5. Salvage: clinical measures for patients by innovating appropriate medicines and therapies

There is currently no specific treatment for the COVID-19 cases. Clinical measures such as early diagnosis, timely reporting, isolation, and supportive treatment are important to tackle the COVID-19 infection (Wu et al., 2020b). According to the "COVID-19 Diagnosis and Treatment Protocol (Trial Eighth Edition, China)", the current treatments mainly include antiviral therapy, respiratory support, immunotherapy, glucocorticoid therapy and traditional Chinese medicine treatment (2020). A consensus by various countries make 18 recommendations as clinical guide, and coagulation dysfunction, thrombin test, anticoagulation therapy, and alternative therapies are also suggested (Song et al., 2020).

Adjuvant therapies include azithromycin, ascorbic acid, corticosteroids, epomethine, sirolimus, tocilizumab, sarilumab and anakinra. Several of these therapies, *e.g.*, tocilizumab and other interleukin-directed therapies, are administered to inactivate the cytokine storm usually seen in disease progression (Wu et al., 2020b). For patients with refractory hypoxemia, WHO recommends extracorporeal membrane oxygenation (ECMO) for respiratory support (WHO, 2020), and convalescent plasma and immunoglobulin G rescue therapies are also recommended (Chen et al., 2020). As the main cause of death with severe COVID-19, coagulation dysfunction is diagnosed and treated together with COVID-19 cases.

In addition to supportive treatment, antiviral therapy is the most widely used in the treatment of the COVID-19 pneumonia. A variety of drugs are currently being used in clinical trials, such as remdesivir, ribavirin, penciclovir, favipivir, narfalimus, nitazoxanide and chloroquine (Wu et al., 2020b). Among them, remdesivir is a broad-spectrum antiviral drug developed in 2017, able to delay the chain termination of nascent viral RNA (Siegel et al., 2017). Remdesivir has achieved gratifying results in the treatment of COVID-19 patients in the United States (Holshue et al., 2020). However, its performance is questioned by WHO and not recommended for COVID-19 patients since Novermber 2020.

Traditional Chinese medicine has accumulated a profound theoretical basis for plague in ancient China and in recent decades. Most COVID-19 patients have mild influenza-like symptoms, and a small number rapidly progress to acute respiratory distress syndrome, respiratory failure, multiple organ failure, and even death (Huang et al., 2020). During the COVID-19 pandemic, traditional Chinese medicine has achieved good performance in clinical practices (Du et al., 2020; Yang et al., 2021), because of one feature that Chinese medicine can adjust the medication according to different symptoms to provide more effective individualized treatment and have distinct effects on different stages of the COVID-19. One advantage of traditional Chinese medicine is that the prescriptions are formulated based on the clinical symptoms instead of causative pathogens to reduce the disease, shorten the course, and inhibit disease deterioration or complications (Jin, 2020). For example, Yinqiao Powder is traditionally used for fever patients, and Sangjuyin is used for severe coughs (Xu and Zhang, 2020). As they have antibacterial and antiviral functions to enhance the immune functions of the upper respiratory tract (Liu et al., 2015), these two prescriptions are successful in treating patients with mild COVID-19 infection by clearing and regulating the lungs, relieving phlegm and cough, and restoring normal lung function (Xu and Zhang, 2020). Another Chinese medicine Lianhua Qingwen Capsule can significantly improve the clinical symptoms of fever, cough, fatigue, sputum expectoration, shortness of breath, chest tightness, and hypoxia in moderate patients, reduce the duration of fever, fatigue and cough, and improve the efficacy of main symptoms (Cheng and Li, 2020; Dingyun and Yang, 2020; Lv et al., 2020; Yao et al., 2020). It has multiple ingredients and targets to act on SARS-COV-2, and the main active components include kaempferol, quercetin and luteolin bind well to Mpro, and indigo, glycyrrhetinic acid and stigmasterol targeting ACE2 protein (Ling et al., 2020). Thus, Lianhua Qingwen Capsule can reduce lung exudate and and stabilize blood oxygen saturation, reducing the use of respiratory support and antibiotics. For convalescent patients, supplemented with Shuanghuanglian Oral Liquid, Jinhua Qinggan Granules, Shufeng Jiedu Capsules, Xuebijing Injection, and other proprietary Chinese medicines can eliminate excess evil in the body, store healthy blood and promote the rehabilitation process (Gong et al., 2020; Xiong et al., 2020; Zhang et al., 2020a; Zhang et al., 2020b).

Regardless the selection of Western therapies or traditional Chinese medicine, the critical thing in *Salvage* strategy is to fundamentally alleviate the symptoms of the COVID-19 patients. The COVID-19 pandemic is the greatest global public health challenge in our generation in an unprecedented way. A transatlantic partnership from Spain, Italy and the United States proposes a standards-based integrated system approach and data-driven framework which provides information for decision-making to manage clinical responses and social interventions, offering opportunities for global standardization and coordination on clinical measures (Ros et al., 2020). It is worth noting that the proposed *Salvage* strategy is suggestive for other emerging infectious diseases with or without effective treatment. The severity of the COVID-19 and future public health crises encourage the data share on global scale, and international cooperation provides opportunities for faster completion and universality of clinical trials around the world. Though it might threaten researchers by the loss of autonomy inherent, their innovative potential might be stimulated for advanced progress (Marshall, 2017).

6. Shield: vaccine development as the ultimate defense to protect healthy crowds from infection

Before a specific drug for the COVID-19 has been developed, vaccine is a life-saving straw for ending this intensifying pandemic. By March 2021, 13 vaccines have been approved and more than 90 candidate vaccines are undergoing clinical trials (Yan et al., 2021). COVID-19 vaccine development uses diverse platforms focusing on nucleic acids, recombinant proteins, virus-like particles, viral vectors, synthetic peptides, and attenuated or inactivated viruses. In the absence of a previously licensed human coronavirus vaccine, there are still further questions about the long-term effectiveness and safety of the COVID-19 vaccine (Lee et al., 2021). The three main vaccine types for the COVID-19 are viral vector, whole virus and mRNA vaccines. According to Airfinity, 43% of all COVID-19 vaccines are mRNA vaccines (>179 million doses by March 2021), followed by whole virus vaccines (35%) and viral vector vaccines (22%). Among them, mRNA vaccine is the most widely used vaccine and composed of genetic materials encoding the protein of SARS-CoV-2 that can cause an immune response (Jackson et al., 2020). It has three main advantages of independence on living cells, fewer substances in the mixture, and lower demand for production capacity (Irwin, 2021). China approves the emergency use of the viral vector and whole virus vaccines for the first time in June 2020 and starts vaccinating since January 2021. The two vaccines of Kexing and Sinopharm are the mainstay of China's domestic vaccination program, and have the advantage of mild cold storage condition at 2–8 °C (Mallapaty, 2021). China plans to complete the vaccination scale of 70% of 1.4 billion people by the end of 2021. Globally, 570 million people have received 1.06 billion doses by 27th April 2021, accounting for about 7.3% of the global populations (Kreier, 2021).

Although the current coverage rate of vaccines is impressive, the unfair and inequitable distribution of vaccines within and between countries challenge its effectiveness (Kreier, 2021). The vaccination rates among rich and poor countries continue to expand, and only less than 1% of people in low-income countries have been vaccinated. It is expected that at least more than 75% of the world's population need to be vaccinated to achieve the herd immunity and control the COVID-19 epidemic. The US government announced on 7th May 2021 the abandonment of patent protection for the COVID-19 vaccine, which is a historic step to expand vaccine supply for people all over the world (Maxmen, 2021). Gathering geographic information on the existing vaccines is therefore essential for vaccine distribution. Nigeria conducted a study to track and map the country's vaccination team using geographic information systems, determining the missing population and expanding the coverage of vaccination (Barau et al., 2014). A cartographic study on 195 countries shows a lack of vaccination coverage in many parts of Africa and Asia, and such geographic information can provide advice to policymakers to ensure equitable vaccination in developing countries (Yau and Gastner, 2021).

Besides COVID-10 vaccines, similar attentions and strategies should focus on vaccines effective for other viruses causing infectious diseases like influenza and respiratory syncytial virus (Thompson et al., 2003) and Hepatitis B virus (Lavanchy, 2004) for their development and delivery to countries under development or facing the outbreak. International cooperation on vaccines for emerging infectious diseases is suggested and vaccine nationalism should be avoided. The establishment of vaccine geographic information systems can help us more intuitive understanding the equitability of vaccination distribution and solve the related problems in backward areas.

7. Conclusion and perspectives

In this review, we explicitly discuss the concept of 5S global biological defense system to tackle the COVID-19 pandemic and other emerging infectious diseases. The biohazard database established by *Sheet* is conducive to the analysis and prediction of global epidemiological trends, thereby establishing a solid defense mechanism. *Surveillance* provides surveillance and prognostication tools to monitor the outbreak and trend of epidemics. *Strategy* represents policies and legislations for personal protection, social distancing, lockdown and trace-track to block the spread of infectious diseases in communities. *Salvage* and *Shield* offer guidance in clinical treatment and achieve fair vaccination for people around the world, respectively. These five strategies from different angles jointly respond to and tackle the current COVID-19 pandemic, and also lay a solid theoretical foundation for the public health problems that may be addressed in the future.

One single strategy may be able to slow down the COVID-19 epidemic, but the combined application of these five strategies is the ultimate solution to stop this crisis. To complete prevention and control of the COVID-19 pandemic, China collects anonymous mobile geolocation data (*Surveillance*) to quantify the impact of physical distancing (*Strategy*) and vaccination (*Shield*), and shares “COVID-19 Diagnosis and Treatment Protocol” guidelines (*Sheet* and *Salvage*), exhibiting a good example of integral 5S strategies as a national biodefense system (Huang et al., 2021a). Evidences by the Susceptible-Exposed-Infected-Removed/Recovered (SEIR) model, the combined use of 5S strategies has achieved better results in reducing transmission, cases and mortality, and effectively curbed the spread of the COVID-19 in China (Geng et al., 2020). To maintain the best balance between various strategies, policymakers must take local economic, cultural and social characteristics, and apply responsive actions in a timely manner to prevent the outbreak and development of other emerging infectious diseases.

Emerging infectious diseases are long-term threats to public health and human society. Fighting against COVID-19 pandemic and other emerging infectious diseases is a long rocky journey. Although some COVID-19 vaccines have been developed and successfully used to protect healthy people, we still face the risks of SARS-CoV-2 mutants and the next wave of other unknown infectious viruses. The global biodefense system has been recently raised by many researchers and governments as a strategic program protecting human society from biohazardous threats, including emerging and re-emerging infectious diseases, biosecurity and food safety. The ultimate goal is to implement local epidemic prevention and assistance programs from point to point, taking the country as the node, and eventually a 5S strategic scheme covering the whole world as a complete global biological defense system.

CRediT authorship contribution statement

Xinzi Wang: Investigation, Data curation, Writing- Original draft preparation. **Tianyun Wu:** Investigation, Data curation, Writing- Original draft preparation. **Luis F.S. Oliveira:** Resources, Writing- Original draft preparation. **Dayi Zhang:** Conceptualization, Funding acquisition, Resources, Methodology, Supervision, Writing- Original draft preparation, Writing-Reviewing and Editing.

Declaration of competing interest

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

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