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Review

An overview for monitoring and prediction of pathogenic microorganisms in the atmosphere



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ABSTRACT

Corona virus disease 2019 (COVID-19) has exerted a profound adverse impact on human health. Studies have demonstrated that aerosol transmission is one of the major transmission routes of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Pathogenic microorganisms such as SARS-CoV-2 can survive in the air and cause widespread infection among people. Early monitoring of pathogenic microorganism transmission in the atmosphere and accurate epidemic prediction are the frontier guarantee for preventing large-scale epidemic outbreaks. Monitoring of pathogenic microorganisms in the air, especially in densely populated areas, may raise the possibility to detect viruses before people are widely infected and contain the epidemic at an earlier stage. The multi-scale coupled accurate epidemic prediction system can provide support for governments to analyze the epidemic situation, allocate health resources, and formulate epidemic response policies. This review first

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elaborates on the effects of the atmospheric environment on pathogenic microorganism transmission, which lays a theoretical foundation for the monitoring and prediction of epidemic development. Secondly, the monitoring technique development and the necessity of monitoring pathogenic microorganisms in the atmosphere are summarized and emphasized. Subsequently, this review introduces the major epidemic prediction methods and highlights the significance to realize a multi-scale coupled epidemic prediction system by strengthening the multidisciplinary cooperation of epidemiology, atmospheric sciences, environmental sciences, sociology, demography, etc. By summarizing the achievements and challenges in monitoring and prediction of pathogenic microorganism transmission in the atmosphere, this review proposes suggestions for epidemic response, namely, the establishment of an integrated monitoring and prediction platform for pathogenic microorganism transmission in the atmosphere.

1. Introduction

Pathogenic microorganisms, including viruses, bacteria, and fungi, can cause infectious diseases [1]. The COVID-19 pandemic has been one of the most threatening public health emergencies worldwide in recent centuries. SARS-CoV-2 is highly capable of mutating, spreading, and immune escape, and thus the medical and health systems in all countries face significant challenges [2–4]. As of March 10, 2023, the rapidly spreading COVID-19 has infected 676,609,955 people and the death toll has reached 6,881,955 [5]. Since the outbreak of COVID-19 worldwide, scientists have focused on SARS-CoV-2 transmission and conducted diverse studies from the perspectives of indoor and outdoor, public places, transportation and so on to develop methods to rapidly contain the pandemic.

Monitoring pathogenic microorganisms in the atmosphere is an important basis for early warning during the initial epidemic stage. However, the current surveillance of cases of infectious diseases mainly relies on manual detection and reporting of cases [6]. Methods including traditional sentinel surveillance, molecular methods in the laboratory, and infected cases surveillance based on big data need to be further supplemented to prevent large-scale epidemic outbreaks [7–9]. Aerosol transmission of SARS-CoV-2 is one of the main reasons for the massive outbreak of COVID-19 [10]. Epidemic outbreaks often occur despite efforts such as isolating incoming passengers and decontaminating or halting shipments of cargo. If viruses can be detected in advance by detecting and monitoring pathogenic microorganisms in the atmosphere, the large-scale outbreak might be prevented earlier [11].

Scientific prediction of COVID-19 development trends based on mathematical modeling is another research focus during the pandemic. Epidemic prediction and early warning have become important references for governments to prevent and control epidemics and thus reduce health threats and economic losses. The need for scientific and accurate epidemic response has drawn increasing attention to the development of epidemic prediction, which is of great concern to the transformation from passive to active epidemic prevention. Models developed around the world differ in model type, acquisition method, hypothesis, and distribution of key input parameters [12]. Existing prediction modeling in the world mainly utilizes epidemiological models such as Susceptible-Exposed-Infected-Recovered (SEIR) and Susceptible-Infected-Recovered (SIR), methods including curve-fitting and machine learning to predict COVID-19 infected cases, mortality and so on [13,14]. However, most prediction models for COVID-19 lack the comprehensive consideration of multiple factors and multi-scale couplings such as atmospheric environment, population density and movement, and economic development.

Therefore, this review emphasizes that the monitoring and prediction of pathogenic microorganisms in the atmosphere is a key point for the rapid perception, early warning and prevention of large-scale epidemic outbreaks by analyzing the impact of atmospheric environment on the survival and transmission of pathogenic microorganisms, sorting out the methods of virus detection and epidemic monitoring, and sum-

marizing the mathematical modeling studies carried out by scholars on epidemics.

2. Pathogenic microorganisms in the atmospheric environment

2.1. Influence of atmospheric environment on pathogenic microorganisms

The infectivity of SARS-CoV-2 in the atmosphere has been proven to be influenced by environmental factors mainly including solar radiation, temperature and humidity, air pollutants. The inactivation of viruses by solar radiation and high temperature, and the phenomenon of fine particles carrying viruses deep into the human lung and so on will inform future mathematical modeling studies and epidemic response [15–18]. Therefore, it is essential to understand the mechanisms by which atmospheric conditions affect the epidemic spread. Moreover, a comprehensive study on the influence of the atmospheric environment on virus transmission is the theoretical basis for improving the monitoring system of pathogenic microorganisms in the atmosphere. Enhanced monitoring of pathogenic microorganisms in the atmosphere could prevent the outbreak of large-scale epidemics.

Studies have demonstrated that SARS-CoV-2 can be transmitted through aerosols [10,11,19–21]. According to experimental data, SARS-CoV-2 can survive and remain infectious in aerosols for several hours [22,23]. The particle size of droplets and aerosols is one of the main factors affecting virus residence time and transmission distance in the air [24]. When the droplet is released into the air together with the virus, the droplet will evaporate into the droplet nuclei due to the decrease in humidity, and the shrinking of particle size will increase the residence time of the virus in the air (Fig. 1) [25–27]. Generally, droplets and aerosols exhaled by humans widely vary in size. The average size ranges of droplet nuclei and droplets generated by coughing are 0.58–5.42 μm , and 0.62–15.9 μm , respectively [28]. The observed median diameter of cough aerosols exhaled by influenza patients and convalescent patients is 0.63 μm [29]. Most of the larger droplets cannot spread far from their origin, quickly depositing on neighboring surfaces and turning them into infectious contamination. The fact that the virus can travel farther through aerosols than droplets is one of the principal factors leading to super-transmission and large-scale epidemic outbreaks [30].

Comprehension of the environmental parameters under which SARS-CoV-2 can survive is a priority in understanding the global spread pattern of COVID-19. Experimental data from one study showed that higher ozone level and temperature, and lower relative humidity are not conducive to the survival of SARS-CoV-2 (Fig. 1) [31]. Moreover, 90% of SARS-CoV-2 is inactivated after 11–34 min of exposure to midday sunlight during summer [32]. Temperature can even affect the virus replication in the host. For example, the rhinovirus that causes the common cold replicates faster at lower nasal temperatures than at warmer lung temperatures [33–35]. In addition to the internal influence on the infectivity and activity of the virus, temperature and humidity also macroscopically affect the distribution of infected cases in different latitudes. According to Huang et al., the distribution of COVID-19 cases varied in

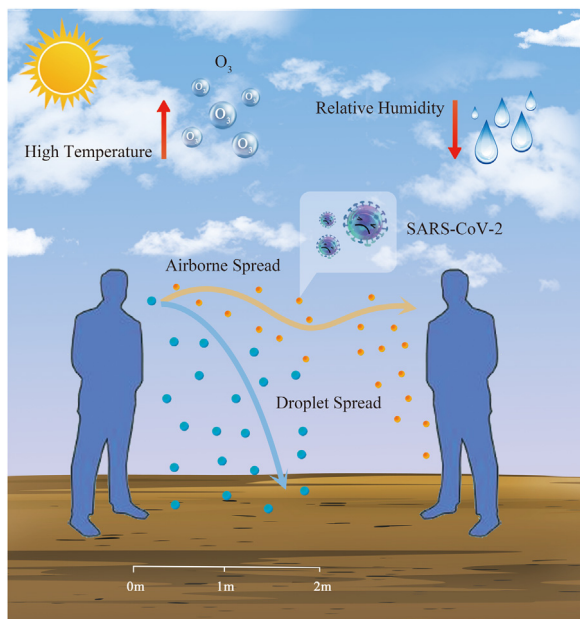


Fig. 1. The spread of SARS-CoV-2 in the atmospheric environment (Modified on the basis of graphical abstract of Yao et al. [31] and Fig. 3 of Božič et al. [25]).

temperature and humidity, 60% of confirmed cases occurred in regions with air temperature ranging from 5 to 15 °C and more than 70% were mainly in areas with absolute humidity of 3–10 g/m³ [36].

Studies have found that 58% of human pathogenic diseases are intensified by climate change. Climate change could also alter the incidence, range, and distribution of vector-borne diseases [37,38]. West Nile virus is mainly transmitted through mosquito bites, and changes in temperature and humidity affect mosquito reproduction and survival [39]. In drier environments, hosts are more susceptible to influenza viruses. Dry air impairs the defenses of the host against influenza infection, reducing tissue repair ability and increasing the susceptibility [40]. Research on the impact of climate change on dengue virus transmission has found that climatic factors including temperature and humidity, and anthropogenic factors including human activities, urbanization, and land use might affect the survival and life cycle of the mosquito. The climate change can also affect the population density of vectors, which in turn affects dengue virus transmission [41,42].

2.2. Environmental pollution and human health

Environmental pollution, especially air pollution, is closely related to human health. Fine particulate matter poses a significant risk to human health by promoting oxidative stress and inflammation, which further contribute to the development of chronic diseases [43–45]. More than 80% of urban residents in the world live in urban areas with an annual average PM_{2.5} higher than 10 µg/m³. The increased risk of diseases including ischemic heart disease (IHD), stroke, and chronic obstructive pulmonary disease (COPD) is associated with long-term exposure to PM_{2.5} [46,47]. PM_{2.5} increases the possibility of respiratory inflammation in COPD patients and also poses a cardiotoxic threat by amplifying the risk of lipid disorders [48,49]. And increased PM_{2.5} concentrations might aggravate the negative effects of depressive symptoms and aging [50]. Particulate matter with a smaller aerodynamic diameter can carry polycyclic aromatic hydrocarbons (PAHs), toxic compounds in the atmosphere that have been linked to inhaled cancer risk [51].

The adverse impacts of air pollution on human health are also reflected in the changes of human susceptibility to COVID-19. The increased susceptibility to COVID-19 has also contributed to the rapid

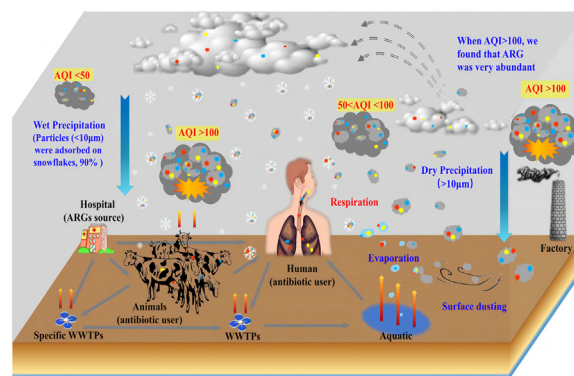


Fig. 2. Schematic representation of the ARGs environmental loop (Fig. 5 of Zhu et al. [64]).

spread of the disease. Studies have also demonstrated that exposure to air pollution is associated with an increased risk of severe illness and death of COVID-19 patients [52,53]. Moreover, it is demonstrated that long-term exposure to NO₂ and PM_{2.5} will cause overexpression of angiotensin-converting enzyme 2 (ACE-2) in respiratory cells [54]. Human cells are more susceptible to SARS-CoV-2 if the expression of ACE-2 and transmembrane protease serine 2 (TMPRSS2) is upregulated. Additionally, exposure to ozone may also increase susceptibility to COVID-19 through the up-regulation of TMPRSS2 expression caused by the unhealthy level of ozone in the environment [55]. Air pollution could also increase the death risk of COVID-19 patients through chronic diseases including cardiovascular and cerebrovascular diseases and cancer [56,57].

In addition to the transmission of pathogenic microorganisms among humans, the production and transmission of pathogenic microorganisms in the environment and among other animals also should be paid more attention. Yu et al. found that the decomposition of meat wastes in daily life such as chicken and pork would lead to the release of high-abundance bioaerosols and pathogenic microorganisms [58]. Additionally, the widespread usage and excretion of antibiotics have caused the spread of antibiotic resistance genes (ARGs) in the environment, which is another risk to the environment and human health. The prevalence of ARGs in bioaerosol is significantly affected by the change in the pathogen community [59]. Current studies have focused on the occurrence, spread, and hazard of ARGs in sewage, sludge, and manure [60–63]. Atmospheric circulation and atmospheric particle transport may contribute to the global spread of ARGs. ARGs from sewage treatment plants, landfills, and hospitals could return to the surface of the Earth through precipitation, especially snow, posing threats to human health (Fig. 2). In winter, air pollution may exacerbate the spread of ARGs in new snow, significantly increasing the health risks associated with air pollution and ARGs [64].

Containment measures for controlling epidemic will also affect industry, transportation, and other human activities, which in turn affect the release of air pollutants and lead to changes in atmospheric composition and atmospheric environment conditions [65]. At the beginning of the COVID-19 pandemic, the implementation of control measures led to a significant decrease in NO₂ and CO₂ emissions, effectively improving urban air quality [66–68]. Megacities in China generally have a population of several million, with high-quality development of transportation, industry, and economy. In January 2020, the concentration of NO₂ in Wuhan City fell by more than 50%, but ozone rose by over 110% [69]. PM_{2.5} concentrations in the Yangtze River Delta and the Pearl River Delta both dropped by more than 40% in the spring of 2020 due to mass closures in transportation and manufacturing [70]. However, reduced nitrogen oxide emissions due to decreased traffic during COVID-19 lockdowns had promoted the formation of ozone and nighttime NO₃ radicals, which promoted the formation of secondary particulate matter

and pollution, triggering hazy pollution [71]. Even if short-term emission reduction cannot cause long-term climate change, the research on the mechanism will provide a theoretical basis for future research regarding climate change.

3. Transmission of pathogenic microorganisms

3.1. Source and transmission of pathogenic microorganisms

Understanding the different routes of virus transmission can facilitate the implementation of a more integrated approach to self-protection. The source of pathogenic microorganisms is usually the natural environment or an infected host, and pathogens transmitted via the environment can live outside the host for hours or even years [72,73]. Pathogenic microorganisms are mainly transmitted from the environment and hosts through contact, aerosol, animal, water, and food to pose threats to human health [74–78]. For example, waterborne diseases can be transmitted through the ingestion of contaminated water, which is a passive carrier of the infection source. Typical waterborne diseases, including cholera and typhoid, often affect human health in densely populated areas [79,80]. Therefore, water treatment plays an important role in reducing the incidence of infectious diseases [81]. Glaciers are also the reservoir of pathogenic microorganisms, with bacteria, algae, archaea, fungi, and other microeukaryotes existing on the glacier surface. Melting glaciers caused by global warming may release ancient viruses that can be released into the environment through different routes [82]. Several unusual snow-originating bacteria can exist and multiply along the hydrological continuum, suggesting that the melting of glaciers triggered by climate warming will affect the microbial diversity of downstream aquatic environments through the hydrological continuum [83]. Climatic and anthropogenic factors also influenced the composition of bacterial communities of glaciers [84].

Epidemics caused by airborne pathogenic microorganisms have been documented. *Aspergillus fumigatus*, variola virus, and varicella zoster virus triggered aspergillosis, smallpox and chickenpox, which were highly contagious and lethal [85–87]. The outbreaks of severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1), influenza A (H1N1), and Middle East Respiratory Syndrome coronavirus (MERS-CoV) and COVID-19 have also posed a major threat to human health [88,89]. The indoor gathering could lead to a high incidence of airborne infectious diseases, and monitoring of pathogenic microorganisms in such an environment can help prevent and control aerosol transmission of viruses (Fig. 3) [90]. Pathogenic microorganisms in indoor air mainly come from breathing and speaking of infected people and outdoors [91]. According to the test data of SARS-CoV-2, the abundance of the virus genetic material in nasopharyngeal fluids is higher than that in feces and urine [92,93]. Crowd gathering is another important cause of the

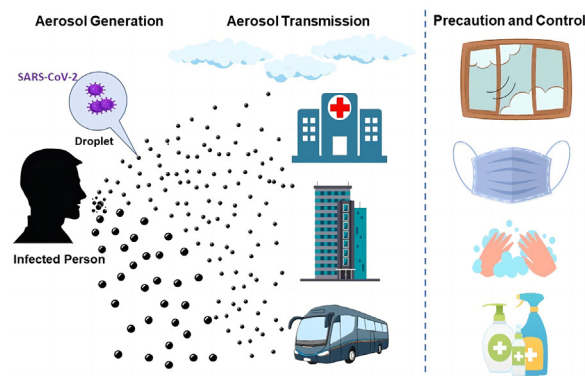


Fig. 4. Aerosol transmission of SARS-CoV-2 and control measures (Graphical abstract of Tang et al. [11]).

COVID-19 outbreak. The impact of common gatherings of less than 100 people on the spread of COVID-19 in cities cannot be underestimated [94].

3.2. Aerosol transmission of SARS-CoV-2 and related countermeasures

The aerosol transmission of SARS-CoV-2 is supposed to be considered in the formulation of prevention and containment strategies (Fig. 4). Studies have provided evidence for the aerosol transmission of SARS-CoV-2, especially in densely populated places. Public places such as restaurants and coffee shops during epidemics are hotbeds for the spread of SARS-CoV-2, especially in winter when people often warm themselves indoors. Eating and drinking without masks and poor ventilation provide the perfect opportunity for the virus to spread [95,96]. The architectural structure should be taken into account when developing a response policy based on the route of virus transmission. The virus could be transmitted through aerosols produced by toilet drains in high-rise residential buildings, which was observed during both the prevalence of SARS and COVID-19 [19]. Given the highly developed modern transportation, the frequency and complexity of emerging infectious diseases will gradually increase. In addition, the cold chain industry has been linked to COVID-19 cases in some countries, and vigilance against virus transmission by cold chain products is important to controlling the spread of the virus [97]. Stricter non-pharmaceutical intervention including closing public entertainment places and controlling crowd gatherings can effectively control the case increase [98]. The control effectiveness of virus transmission will be improved via the implementation of multiple epidemic control policies [99]. The implementation of the epidemic control measures will gain more time for scientists to conduct relevant research and for governments to develop long-term measures for preventing the epidemic outbreak [100].

Public transport is essential for modern life, while the relatively enclosed space and the high population density in public transportation could facilitate the spread of COVID-19 [101]. Exploring the physical processes of virus transmission in public transportation systems is crucial for the development of control measures targeting population movement [102]. Ventilation plays an important role in curbing the indoor COVID-19 spread. Research has found that insufficient supply of clean air, long exposure time, and inappropriate airflow modes are the main causes of rapid spread of SARS-CoV-2 in densely populated places [103]. Ou et al. studied the ventilation rate threshold for airborne transmission of SARS-CoV-2 and found that poor ventilation below 3.2 L/s is one of the major factors of the COVID-19 outbreak in buses [104]. Current airline cabin ventilation systems may also facilitate the spread of airborne infections [105]. Additionally, using toilets on aircraft may also pose a risk of infection. SARS-CoV-2 may persist in toilets because the virus has been detected in the feces and urine of COVID-19 cases. Passengers could become infected by inhaling aerosols produced in the toilet

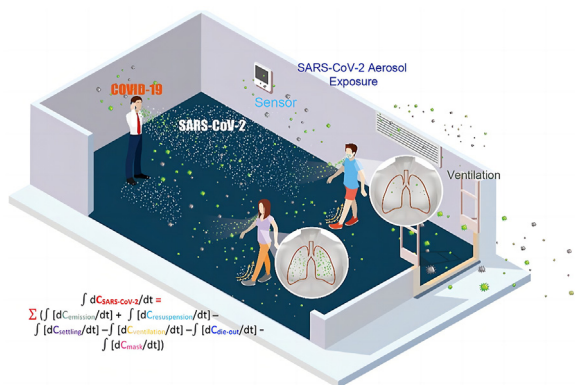


Fig. 3. SARS-CoV-2 aerosol transmission and detection (Graphical abstract of Yao [90]).

during flushing [106]. Therefore, it is crucial to elucidate the airflow field and particulate pollutant distribution in the cabin of vehicles. Validated computational fluid dynamics (CFD) models are frequently and effectively utilized to investigate air distribution and contaminant transportation [107].

4. Monitoring methods of pathogenic microorganisms in the atmosphere

4.1. Virus monitoring methods during COVID-19 pandemic

The ability to detect and monitor pathogenic microorganisms early is essential in determining the scale of an epidemic. The usage of cell culture to isolate pathogens is a traditional virus detection and analysis method. Although this method can distinguish the activity and type of viruses, its operation is complicated and time-consuming, requiring high technical expertise [108]. In the COVID-19 pandemic, molecular methods including reverse transcription-polymerase chain reaction (RT-PCR), isothermal nucleic acid amplification, nucleic acid hybridization using microarray, and amplicon-based metagenomic sequencing have been utilized to detect viruses [109–111]. The development of antigens and nucleic acids for virus detection has further improved the ability and convenience of rapid detection of viruses in outbreaks and has been widely used in the COVID-19 pandemic. However, SARS-CoV-2 antigen detection might present a relatively high probability of false positive in the low epidemic prevalence, thus it is usually regarded as a supplement for nucleic acid detection [112]. In order to detect SARS-CoV-2 nucleic acid sensitively and rapidly, a CRISPR/Cas12a-based assay with a naked eye readout, CRISPR/Cas12a-NER, has been developed. This method has high consistency with qPCR detection, which can detect as

few as 10 copies of the virus gene in 45 min [113]. Serological testing provides essential information for developing vaccines, determining antibody prevalence and infection in the community. This method can also identify previous infections, even if tests are not conducted during epidemics [114].

In recent years, exhaled breath has become an important biomarker for disease analysis. Volatile organic compound (VOC) biomarkers in exhaled breath will play an important role in diagnosing respiratory infections. The real-time monitoring of VOC released by life metabolism is expected to reveal multiple vital environmental health problems of aerosol exposure [115]. In order to timely monitor whether humans are infected with SARS-CoV-2 and avoid the reintroduction of infectious sources into humans and the environment, Chen et al. utilized breath-borne VOC for immediate screening of COVID-19 and adopted machine learning models to distinguish COVID-19 from other test subjects (Fig. 5) [116]. Moreover, Shen et al. integrated electronically addressable silicon nanowire (SiNW) sensor devices, microfluidics and bioaerosol-to-hydrosol air sampling techniques for real-time monitoring of airborne influenza viruses, as well as airborne SARS-CoV-2. The system translates airborne biohazard into a viewable electrical signal, enabling humans to sense the airborne biohazard (Fig. 6) [90,117]. The rapid transmission of airborne pathogenic microorganisms reminds us that the monitoring of pathogenic microorganisms in the atmosphere is significant to fighting against large-scale infectious diseases [118]. Therefore, it is of particular significance to monitor bioaerosols including viruses and bacteria, which is an important supplement to the existing monitoring methods of viruses and relevant epidemics. The impact of the COVID-19 pandemic will promote the emergence of bioaerosol monitoring instruments with higher flux, faster detection, and greater sensitivity.

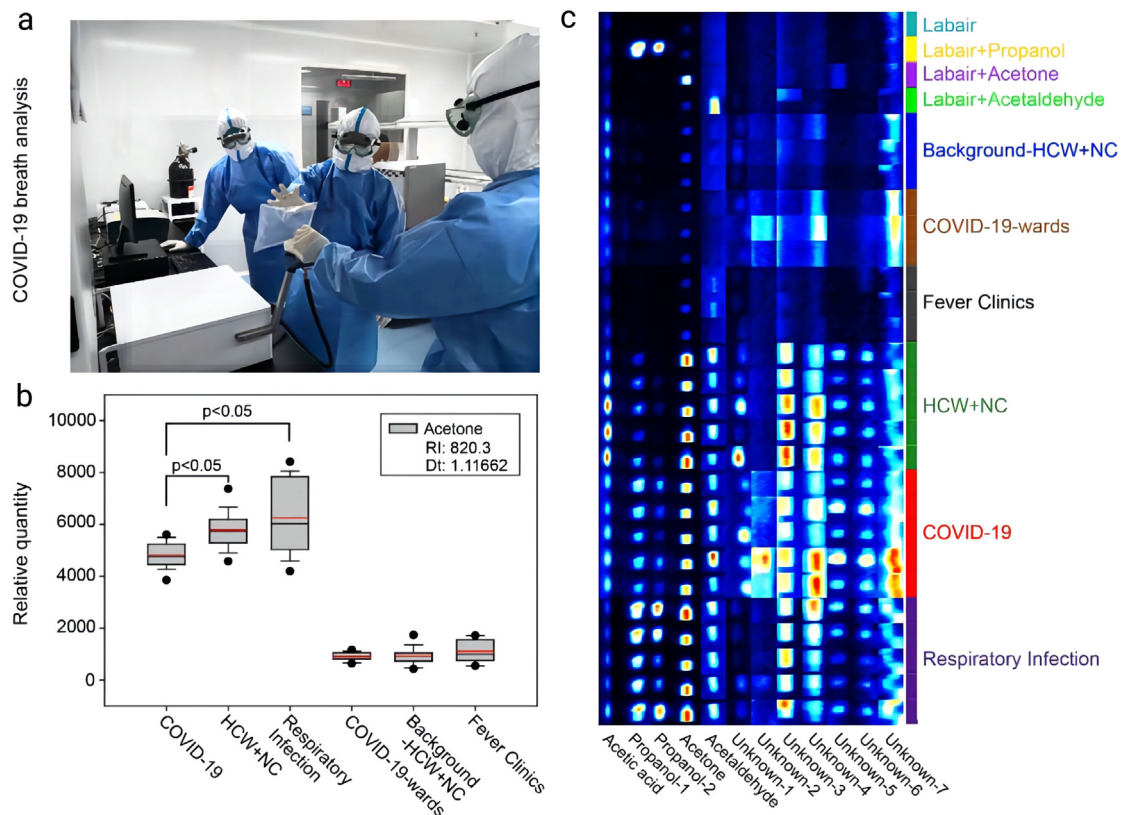


Fig. 5. (a) Breath-borne VOC analysis using GC-IMS in a certified CDC level-2+ biosafety lab; (b) boxplots (from top to bottom: outlier, 95% percentile, mean, median, 5% percentile, and outlier) of acetone in exhaled breath samples collected from different subject groups (74 COVID-19, 87 (HCW + NC), 30 RI, 59 COVID-19 wards, 19 backgrounds of HCW + NC, 9 fever clinics); (c) representative samples of GC-IMS signals of 12 VOC species detected in the exhaled breath and background air samples of different groups (Fig. 1 of Chen et al. [116]).

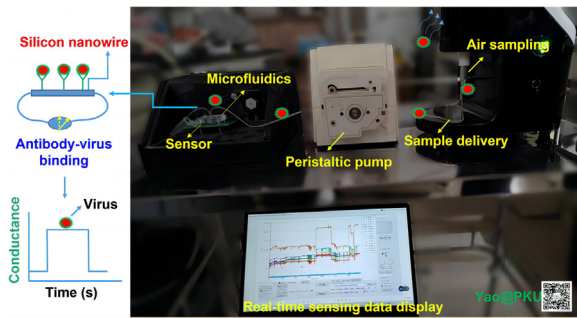


Fig. 6. Integration of commercialized technologies, including air sampling, microfluidics, and antibody-decorated silicon nanowire sensor for real-time monitoring of SARS-CoV-2 aerosol (Fig. 1 of Yao [90]).

4.2. Bioaerosol and its monitoring methods

Bioaerosols, mainly consisting of viruses, bacteria, fungi, pollen, and cell debris, account for 30%–80% of particulate matter in the atmosphere. Meteorological conditions and seasonality may cause changes in the concentration, abundance, and diversity of microorganisms in the atmosphere [59]. Bioaerosols originate from a wide range of natural sources and human activities. Long-distance transport of bioaerosol exerts significant impacts on ecosystems, human health, agricultural productivity, and climate change. External forces such as wind and water can promote the release of bioaerosols from soil and water into the air. Some animals release pathogenic microorganisms in the air and transmit diseases to other animals or humans through bioaerosol. Geographic locations and land-use type also affect bioaerosol diffusion (Fig. 7) [119]. Therefore, the detection and monitoring of bioaerosols containing viruses and bacteria is a significant frontier in protecting human health. Most current samplers use filtration, impaction, impingement, and electrostatic precipitation as the core technology [120–123]. Analysis methods based on the inertia principle, cultivation, and microscope are the most commonly used methods for bioaerosol detection. However, these methods may affect the activity of the target microorganism during sample collection while the target bioaerosol that can be cultured is limited and the cultivation-based analysis method is more time-consuming [124]. Deoxyribonucleic acid (DNA) and adenosine triphosphate (ATP) are present in all biologically active microorganisms, and

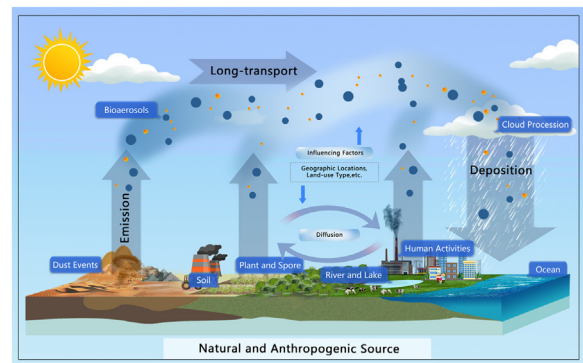


Fig. 7. The source and transport of bioaerosols (Modified on the basis of graphical abstract and Fig. 2 of Xie et al. [119]).

this advantage has led to the development of DNA-based and ATP-based bioaerosol detection technologies, including DNA extraction techniques, DNA quantification devices, DNA sequencing techniques, and ATP bioluminescence detection [125–127].

The further development of bioaerosol monitoring methods is an important support for monitoring the occurrence and spread of major epidemics. Laser-induced fluorescence (LIF), laser-induced fluorescence light detection and ranging (LIF LIDAR), mass spectrometry, and surface-enhanced Raman spectroscopy are classical online methods for the real-time detection of bioaerosol. Bioparticles include chemical substances that fluoresce when excited with UV radiation, and this property promotes the application of lasers in real-time monitoring of bioaerosols [128]. The LIF LIDAR method improves the detection range and spatiotemporal resolution of bioaerosol detection in real-time [129]. On-line analysis of biological particles by particle beam mass spectrometry has provided a key method in the chemical detection of biological aerosols [130]. Since scientist Raman first observed the Raman effect in 1928, Raman spectroscopy and surface-enhanced Raman spectroscopy have been developed and utilized to characterize bioaerosols [131,132]. The detection and analysis methods described above are fruitful scientific achievements of bioaerosol monitoring methods, but these developing methods inevitably have limitations. The accuracy of real-time detection methods which are suitable for monitoring large-scale samples still needs to be further improved. The improvement of

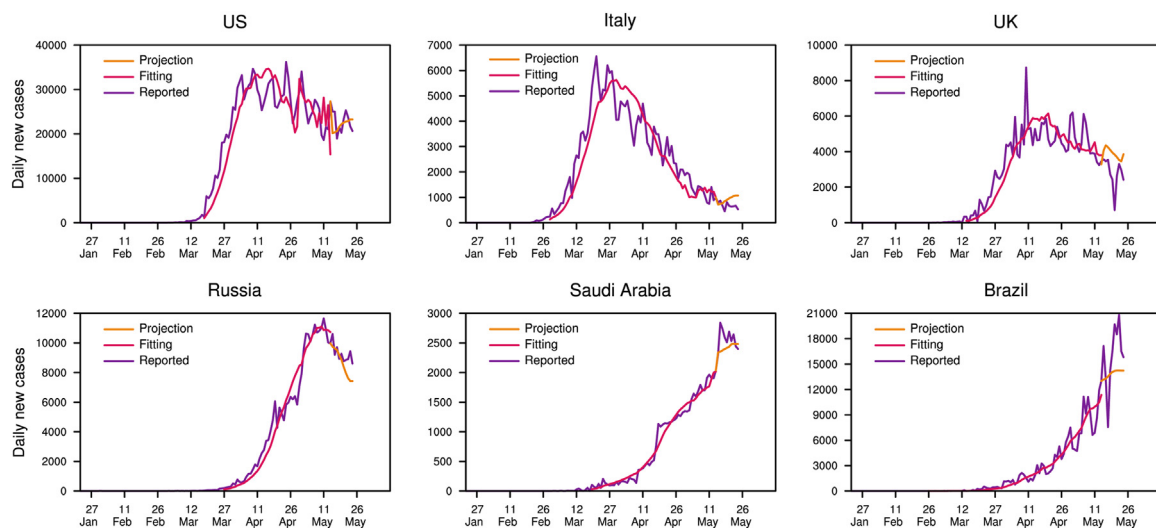


Fig. 8. Time series of the number of new cases per day in six countries (USA, Italy, UK, Russia, Saudi Arabia, and Brazil) between January 22 and May 24, 2020. The numbers of reported confirmed cases for the same period are shown by violet lines, whereas the simulated cases (January 22–May 14, 2020) and hindcast cases (May 15–24, 2020) are shown by dark pink and orange lines, respectively (Fig. 2 of Huang et al. [147]).

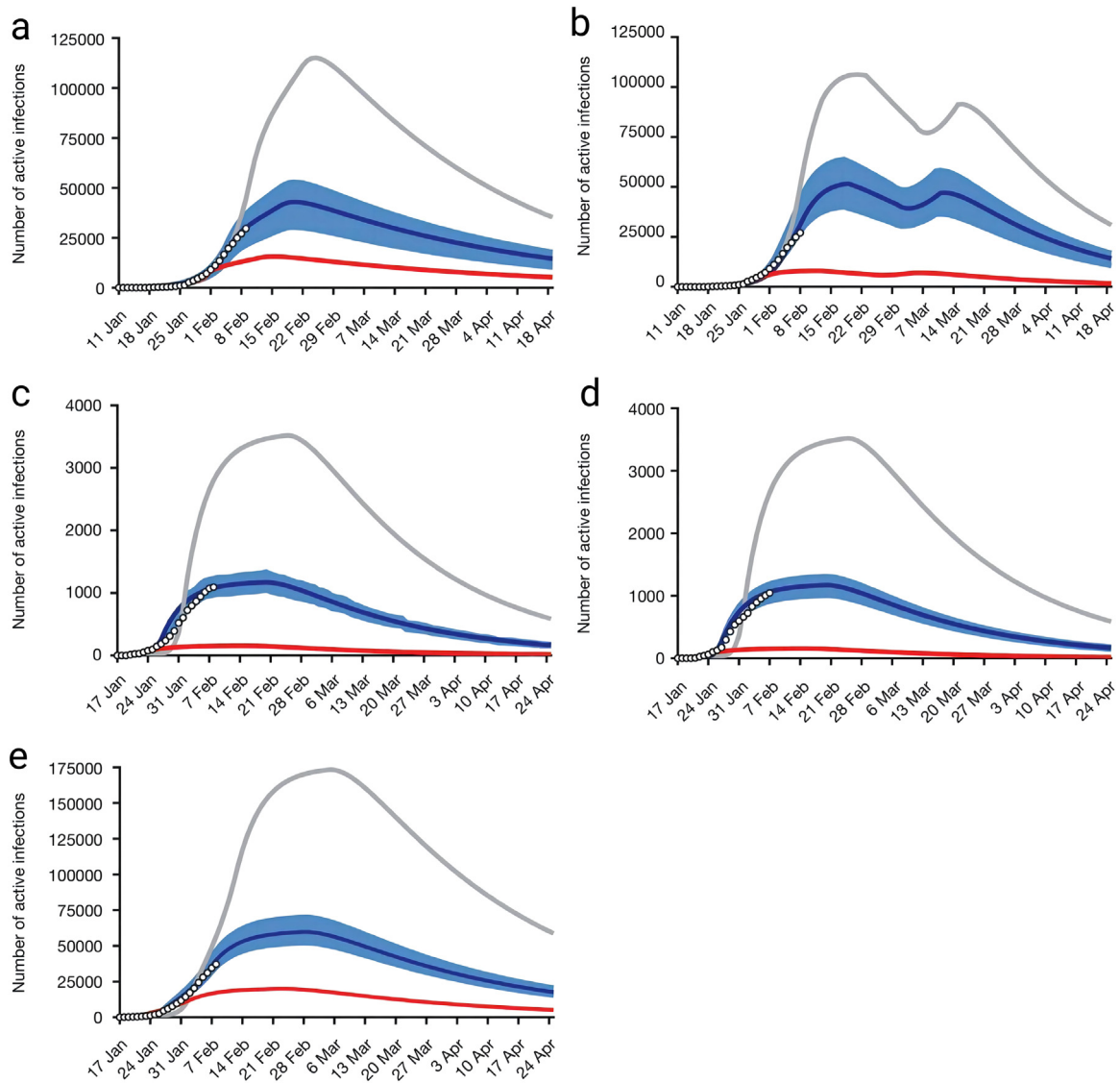


Fig. 9. Number of active infections predicted by the modified SEIR model for (a) Hubei province under strict quarantine, (b) Hubei province under eased quarantine, (c) Guangdong province, (d) Zhejiang province and (e) China when interventions were introduced on January 23 (blue), five days later (gray) and five days earlier (red). Actual data of daily confirmed infections were fitted onto the curve (circles). SEIR, Susceptible-Exposed-Infectious-Removed (Fig. 2 of Yang et al. [154]).

bioaerosol monitoring methods also needs to overcome the difficulties of complex chemical components and multiple interference sources in the environment.

5. Global multi-scale epidemic prediction model and system

5.1. Mathematical methods in epidemics

Mathematical methods and models are important tools for the public health research of host, pathogen, and disease transmission characteristics in infectious diseases. In addition, mathematical methods and models can be utilized to evaluate epidemic response policies [133]. Nowadays, based on advances in data acquisition methods and evolving algorithms and theories, increasingly detailed and accurate parameterization schemes have enhanced the ability of infectious disease models to predict epidemic spread [134]. In the 21st century, mathematical modeling has an increasing influence on the public health field. During the prevalence of SARS in 2003, various mathematical models played an important role in describing the transmission characteristics of the

disease and evaluating the effectiveness of prevention measures. The important parameters of the epidemic were obtained, and the parameter identification method based on the actual cases was developed, which improved the consistency between the simulation results and the actual data [135,136]. In addition to describing the transmission characteristics of the H1N1 influenza A virus and the impact of prevention and control measures on the epidemic spread based on mathematical models, scholars also analyzed the influenza kinetics in the host by establishing small-scale models [137]. Identifying intermediate hosts is also significant for mitigating the negative effects of infectious diseases. During the COVID-19 pandemic, scholars have also proposed a mathematical model to identify possible intermediate host species of emerging zoonoses based on ecological data of species and epidemiological data of pathogens [138]. Mathematical models could also inform the development, licensing, and decision-making of SARS-CoV-2 vaccines [139].

Accurate prediction of the epidemic could serve as a significant reference for ensuring human life safety, response policy formulation, medical resources allocation, and economic loss reduction [12,140]. Therefore, it is important to characterize the epidemic transmission

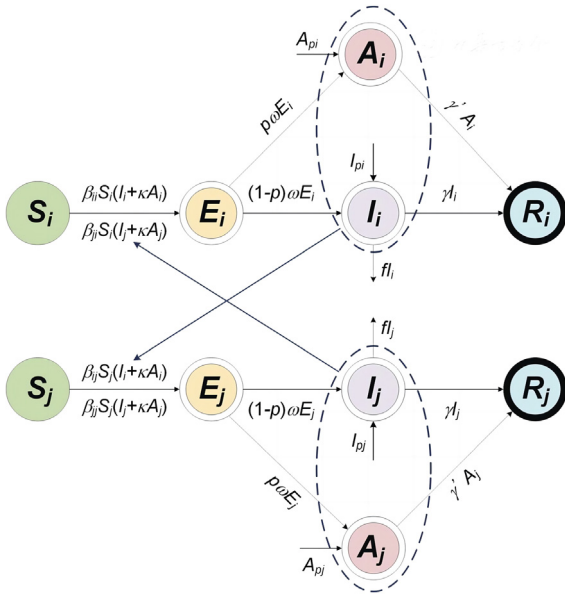


Fig. 10. Flowchart of the age-specific SEIAR model. i and j represent age ≤ 14 , $15-44$, $45-64$, and ≥ 65 , respectively ($i \neq j$) (Fig. 1 of Zhao et al. [156]).

dynamics in multi-scale scenes. The prediction models and methods utilized in countries are mainly based on the SIR or SEIR model, long short-term memory (LSTM) technique, auto-regressive integrated moving average (ARIMA) model, machine learning, statistical analysis, etc. [141–145]. Scholars suggest that climate modeling methods should be adopted to render COVID-19 predictions more reliable, as approaches including Bayesian tools and ensemble modeling techniques have improved the reliability of climate models [146]. It is of great significance to establish a multi-scale coupling model to predict the development trends of emerging infectious diseases, which can also reflect the effectiveness of response measures on epidemic containment.

5.2. Epidemiological model development during the COVID-19 pandemic

During the early stage of the COVID-19 pandemic, the Global Prediction System for COVID-19 Pandemic (GPCP) established by Lanzhou University combined the statistical-dynamic climate prediction methods of atmospheric sciences with epidemiological models, featuring multi-disciplinary strengths [147–149]. On the basis of actual epidemic data, GPCP conducts daily, monthly and seasonal predictions of COVID-19 cases in countries worldwide, taking into account the impact of environmental factors including temperature and humidity, as well as non-pharmaceutical interventions on the epidemic development trend. The prediction of GPCP for the epidemic development trend, the peak of daily new cases and the cumulative cases of COVID-19 provides an important reference for understanding the epidemic situation. GPCP can capture systematic variation in the number of daily new cases, and present a good simulation of the oscillation of the number of cases (Fig. 8) [147]. This system also quantified the seasonality of COVID-19. The study found that both the infectivity and mortality of SARS-CoV-2 were higher in colder climates, and this seasonal characteristic was more significant at higher latitudes [150]. In addition to environmental and meteorological factors, anthropogenic factors and other natural factors also play an important role in the COVID-19 pandemic on different time scales. Hence, it is necessary to conduct attribution analyses of the causes and transmission mechanisms of COVID-19 [151]. Predictions of GPCP for the development trends of the five major variants (Alpha, Beta, Gamma, Eta, and Delta) of SARS-CoV-2 in the worst-hit countries also served as an important reference [152].

The Coronavirus Disease 2019 Forecasting System (Beta) was developed by the National Respiratory Medicine Center of First Affiliated Hospital of Guangzhou Medical University, Guangzhou Institute of Respiratory Health, and National Clinical Research Center for Respiratory Disease. Epidemic predictions are conducted for all countries in the world, and modules including case analysis and vaccine progress tracking have been incorporated to conduct accurate epidemic predictions and identify high-risk areas [153]. Based on the domestic migration data and epidemiological data of COVID-19 at that time, Yang et al. introduced the

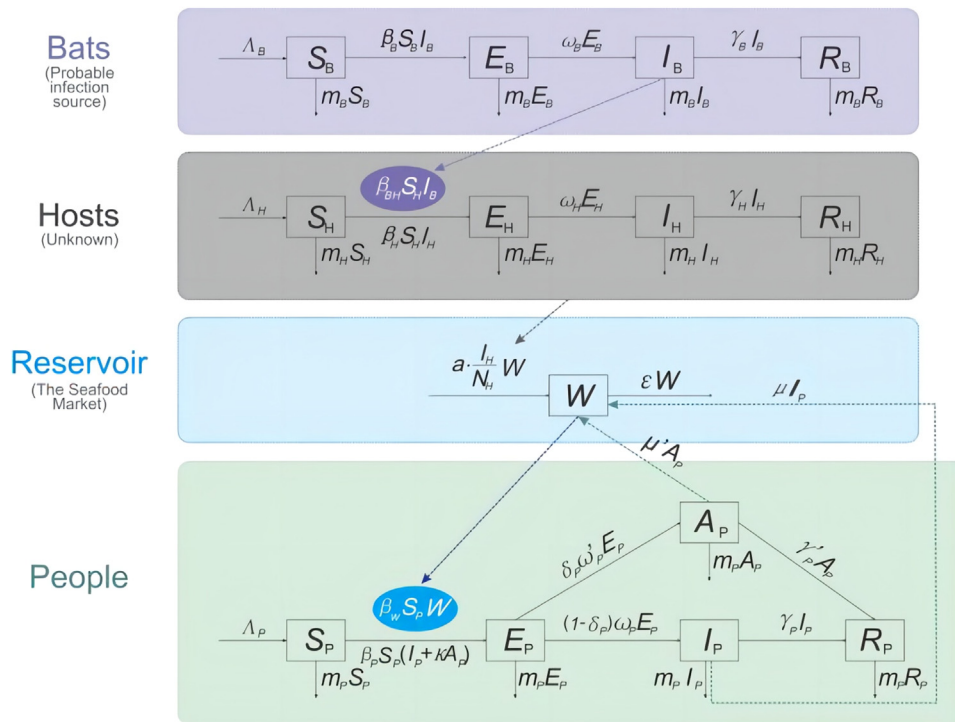


Fig. 11. Flowchart of the Bats-Hosts-Reservoir-People transmission network model (Fig. 1 of Chen et al. [158]).

contact rate before and after the implementation of the control policy to improve the SEIR epidemiological model to predict the epidemic development [154]. The improved model showed the impact of early and late interventions on the number of infections and predicted the peak and end time of epidemic waves, as well as the cumulative number of cases in several provinces in China. According to their simulations, if the control measures had been delayed by 5 days, the scale of the epidemic would be increased three-fold (Fig. 9) [154]. The model developed by Vespignani et al. also showed that the epidemic emergency response implemented in China avoided hundreds of thousands of COVID-19 cases during the early stage of the pandemic [155].

In order to comprehend the morbidity risk of COVID-19 in individuals of various age groups, Zhao et al. based on the SEIR model, established a five-compartment SEIAR model with asymptomatic patients added. In the study, COVID-19 patients were divided into different age groups, with each group classified into local cases and imported cases from outside the province. Based on the above methods, it was concluded that SARS-CoV-2 has high transmissibility among middle-aged and elderly people who are over 45 years old and should pay more attention to self-protection (Fig. 10) [156]. The spread of SARS-CoV-2 caused by cross-regional population movements has brought challenges to the prevention and control of the epidemic. The risk of epidemic transmission in small and medium-sized cities can also be described using mathematical methods. By developing the urban epidemic hazard index (EpiRank), Li et al. found that small towns posed greater epidemic hazards due to the large local population and small inter-city transportation [157]. Moreover, it is also significant to understand the potential transmission of the infection source to humans. A Bats-Hosts-Reservoir-People transmission network model developed by Chen et al. simulates the potential spread from the infection source (probably be bats) to humans, and also facilitates the comprehension of COVID-19 transmissibility worldwide (Fig. 11) [158].

6. Conclusion and suggestion

The frequent emergence of emerging infectious diseases poses a serious threat to human life. Increasingly intimate associations between human society and the natural environment are driving the emergence of novel pathogens. These pathogens existed within complex ecological systems that are characterized by trophic interactions between hosts, vectors, and the environment. It is essential to comprehend the relationship between microorganisms and human health from an ecosystem perspective. The atmospheric environment is one of the vital fields of biological research. However, the composition and diversity study of pathogenic microorganisms in the atmosphere needs to be further developed, and the functional potential of the microbiome is expected to be further explored. In general, the combined effects of the various factors and the weight of their respective effects on pathogen transmission need further clarification. Studies on the impact of extreme events, global large-scale and long-term monitoring and prediction of epidemics are not fully developed. In addition, the research on the temporal and spatial distribution of pathogenic microorganisms driven by climate and environmental factors, their adaptability to climate and environmental changes, and the rule of their genome evolution need to be further promoted. Combining the knowledge introduced in this review, the following suggestions are listed in response to the above questions.

Firstly, research on the core influencing factors of climatic environment on pathogen transmission should be strengthened. This includes expose-response relationships, interaction patterns, and cause-and-effect relationships of climatic environment and pathogen transmission, which is critical to understanding the distribution of pathogenic microorganisms across different environments, spaces, and populations. A variety of viruses have been found in grasslands, forests, wetlands, frozen soils, glaciers [159–162]. The Arctic and Antarctic regions also contain a wide variety of pathogenic microorganisms

[163]. The thawing of frozen soil could also activate long-dormant pathogenic microorganisms and influence the abundance and diversity of pathogenic microorganisms [164,165]. Currently, more than 60% of human pathogens are zoonotic while reverse zoonoses have the potential to cause the virus to evolve and affect the effectiveness of vaccines [166,167]. Therefore, experimental systems should be constructed based on epidemiology, atmospheric sciences, environmental sciences, evolutionary genomics, bioinformatics and artificial intelligence to study the synergistic effects of multiple climatic factors on the activity, genome mutation, cross-species transmission, adaptation and evolution of pathogenic microorganisms.

Secondly, sensitive and short-cycle methods for the collection and monitoring of pathogenic microorganisms in atmospheric environment should be further developed. Quantitative research that directly measures the concentration of aerosolized pathogenic microorganisms has limitations. Meanwhile, microbial detection and analysis technologies are also developing. For example, the portable high-capacity cyclone sampler Yao-CSpler presented stable microbial collection performance for bacteria, fungi, and even viruses. Cryo-electron tomography (cryo-ET) method revealed the features of SARS-CoV-2, which laid a good foundation for virus detection and analysis [168,169]. The continuous development of automation technology holds particular promise for the exploration of pathogenic microorganisms in the atmosphere. In the future, more convenient and sensitive detection technology and tools for pathogenic microorganisms are expected to be developed. A real-time monitoring network should be established to monitor pathogenic microorganisms in the atmosphere at key places in cities, providing data and information support for early detection and early warning of epidemics.

Thirdly, it is significant to establish an integrated monitoring and prediction platform for epidemics by combining multidisciplinary research forces. From the perspective of research methods, the multidisciplinary cooperation and innovation of epidemiology, atmospheric sciences, environmental sciences, sociology, demography, etc. are supposed to be fully promoted. With respect to population vulnerability and susceptibility, the human health risks from climate change should be identified, and the pathogenic mechanism of climate change affecting human health should be elaborated. In addition, the social nature of humans and multiple relevant factors are supposed to be given full consideration. Therefore, it is important to establish an accurate epidemic prediction system with multiple factors and scales, including epidemic, environment, weather, climate, population, transportation, economy, and society. This system will simulate the epidemic development trend under different scenarios and response measures, evaluate the impact of the epidemic, and formulate the optimal epidemic response policies. The establishment of an integrated monitoring and prediction platform for epidemics is an essential support to comprehensively improve epidemic prediction and emergency decision-making, which is also of great significance for future epidemic response.

Declaration of competing interest

The authors declare that they have no conflicts of interest in this work.

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