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COVID-19: A Year Long and Beyond?

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In December 2019, a number of patients with pneumonia of unknown etiology (PUE) were reported in Wuhan, Hubei Province (1). The coronavirus disease 2019 (COVID-19), caused by a virus also known as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), was identified by China in January 2020. On January 30, 2020, the World Health Organization (WHO) declared coronavirus a public health emergency of international concern (PHEIC), and on March 11, it announced that COVID-19 could develop into a global pandemic (2–3). As of February 8, 2021, there had been 105,805,951 confirmed cases, 2,312,278 confirmed deaths, and 223 countries, areas or territories were effected (4).

Through one year's efforts, different countries around the world achieved varying results in pandemic control. In some countries like China, the pandemic has been well controlled, while in other countries the situation is still grim.

China initiated a national campaign against COVID-19 immediately after identifying this new virus. In around two months, the daily increase in domestic cases fell to single digits; and in approximately three months, a decisive victory was secured in the battle to defend Hubei Province and its capital city of Wuhan (5). The overarching strategy was early containment, and the key was active case identification and management (6). "Four Earlies" (early detection, early reporting, early isolation/quarantine, and early treatment) were the primary requirements for the implementation of all control measures. All communities, organizations and citizens were mobilized to participate in pandemic prevention and control (7–8). Then a suppression strategy was implemented by establishing a strong and flexible response mechanism, implementing, or lifting control measures based on the results of surveillance and risk assessment in different regions. Now we have entered the late stage of suppression.

In the winter and spring season of 2020–2021, large-scale local outbreaks were detected in the rural areas of Hebei, Jilin, and Heilongjiang provinces, and more than 2,000 cases were reported in total (9–10). After unremitting efforts of containment and suppression, the local outbreaks were successfully controlled.

As of January 2021, more than 230 COVID-19 candidate vaccines had been in clinical or pre-clinical development globally (11), including inactivated or live virus vaccines, virus vectored vaccines, protein subunit vaccines, nucleic acid vaccines (mRNA and DNA), virus-like particles, and nanoparticles, each having discrete advantages and shortcomings. China has chosen 5 platforms to develop COVID-19 vaccines. As of February 3, 2021, 31 million doses of inactivated COVID-19 vaccines had been administered in China, targeting high-risk groups, including healthcare/frontline personnel, essential workers who are critical to maintain the social performance, cold-chain industry employees and people working or studying overseas (12). As vaccination started smoothly and progressed as scheduled, China CDC has been closely monitoring vaccination coverage and adverse events following immunization (AEFI). The data shows that the reported rate of serious adverse events is no higher than that of the influenza vaccine, reflecting the fact that the currently used inactivated COVID-19 vaccines (13) are safe. This is because the Chinese government has always made the safety and efficacy of COVID-19 vaccines a priority and the Chinese vaccine manufactures are pushing forward vaccine development in strict scientific and regulatory process; 2021 will be a year of vaccination against COVID-19 among broad populations based on the strategy of prioritization. COVID-19 vaccines have raised hope of reducing infected cases and virus transmission and getting life back to normal soon.

Looking into the future, there will still be many uncertainties in 2021. One of them is that the COVID-19 pandemic might become a lasting epidemic or endemic. Furthermore, many new characteristics of COVID-19 have been reported, such as long-term sequelae, reinfection, reoccurrence of viral RNA, and long-time or intermittent latency.

Therefore, although we have developed vaccines, there are still many uncertainties. The emergence of new virus variants of concern (VOC) leading to increased transmissibility and deteriorating epidemiological situations have brought greater challenges, leaving us a lot of work to do. When facing a new virus, mankind still needs to keep doing research and develop a deeper understanding of it.

Our sincere gratitude goes to the 15 internationally renowned health experts who we invited to give their comments on the COVID-19 pandemic from different aspects on *China CDC Weekly*. They shared their insights and experience in the fight against the pandemic from different perspectives as well as the latest scientific thoughts, while advocating more open and inclusive international cooperation and assistance in the prevention of pandemics in the future.

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REFERENCES

1. The 2019-nCoV Outbreak Joint Field Epidemiology Investigation Team, Li Q. An outbreak of NCIP (2019-nCoV) infection in China — Wuhan, Hubei Province, 2019?2020. China CDC Wkly 2020;2(5): 79 – 80. http://dx.doi.org/10.46234/ccdcw2020.022.
2. Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. Lancet 2020;395(10223):470 – 3. http://dx.doi.org/10.1016/S0140-6736(20)30185-9.
3. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19-1 April 2020. Geneva, Switzerland: WHO; 2020. https://prais.paho.org/es/28863-2/.
4. World Health Organization. Coronavirus disease 2019 (COVID-19) situation report-54. Geneva, Switzerland: WHO, 2021. 1. https://www. who.int/docs/default-source/coronaviruse/situation-reports/20200314-sitrep-54-covid-19.pdf?sfvrsn=dcd46351_2. [2021-2-9].
5. The State Council Information Office of the People's Republic of China. Fighting Covid-19: China in action, June 2020. http://www.scio. gov.cn/ztk/dtzt/42313/43142/index.htm. [2021-2-9]. (In Chinese).
6. Li ZJ, Chen QL, Feng LZ, Rodewald L, Xia YY, Yu HL, et al. Active case finding with case management: the key to tackling the COVID-19 pandemic. Lancet 2020;396(10243):63 – 70. http://dx.doi.org/10. 1016/S0140-6736(20)31278-2.
7. Zhou L, Wu Z, Li Z, Zhang Y, McGoogan JM, Li Q, et al. One hundred days of coronavirus disease 2019 prevention and control in China. Clin Infect Dis 2021;72(2):332 – 9. http://dx.doi.org/10. 1093/cid/ciaa725.
8. Li ZJ, Gao GF. Strengthening public health at the community-level in China. Lancet Public Health 2020;5(12):e629 – 30. http://dx.doi.org/ 10.1016/S2468-2667(20)30266-8.
9. Qi SX, Zhao X, Hao P, Liu NK, Gao GF, Song Y, et al. Two reemergent cases of COVID-19 — Hebei province, China, January 2, 2021. China CDC Wkly 2021;3(2):25 – 7. http://dx.doi.org/10.46234/ ccdcw2021.006.
10. Zhou L, Yao LS, Hao P, Li C, Zhao QL, Dong HL, et al. COVID-19 cases spread through the K350 train — Jilin and Heilongjiang Provinces, China, January 2021. China CDC Wkly 2021;3(8):160 – 2. http://dx.doi.org/10.46234/ccdcw2021.026.
11. World Health Organization. Landscape of novel coronavirus candidate vaccine development worldwide. Geneva, Switzerland: WHO; 2021. https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines. [2021-2-09].
12. National Health Commission of People's Republic of China. Press Conference of the State Council Joint Prevention and Control Mechanism. Feb 4, 2020: Introducing the People's Local New Year's Service Guarantee Related Information.http://www.nhc.gov.cn/xwzb/ webcontroller.do?titleSeq=11368&gecstyp=1. [2021-2-9]. (In Chinese).
13. National Health Commission of People's Republic of China. Press Conference of the State Council Joint Prevention and Control Mechanism. Jan 31, 2020: Introducing the People's Local New Year's Service Guarantee Related Information. http://www.nhc.gov.cn/xwzb/ cwebcontroller.do?titleSeq=11367&gecstyp=1. [2021-2-9]. (In Chinese).

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Preplanned Studies

Mobility Trends and Effects on the COVID-19 Epidemic — Hong Kong, China

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Summary

What is already known about this topic?

Several outbreaks of coronavirus disease 2019 (COVID-19) occurred in Hong Kong in 2020, and the response had varied results based on the strength of policy measures and on compliance of the population.

What is added by this report?

By analyzing data of COVID-19 cases in Hong Kong, combined with the Google Mobility Trends and Oxford COVID-19 Government Response Tracker, we make recommendations for the future prevention and control of the epidemic in Hong Kong.

What are the implications for public health practice?

Monitoring data reflecting multiple aspects, such as the epidemic situation, the mobility behavior of people, and government policy, is helpful for public health practitioners and policymakers to understand the interaction between various factors and to precisely adjust COVID-19 control policies.

Hong Kong is a major port city that lies to the south of Shenzhen City of the mainland of China and acts as an important hub for international exchange. Hong Kong has a high population density and has difficulty controlling respiratory infectious diseases as a result. Though the medical standards in Hong Kong are comparatively good, the fluctuations in the coronavirus disease 2019 (COVID-19) epidemic, which peaked in mid-December 2020 (1), in Hong Kong placed great pressure on the hospital capacity as mobile cabin hospitals had to be used to supplement the situation (2). Accordingly, the testing capacity of Hong Kong has increased, and a peak was reached in September and is still expected to increase (3). Strict policies have helped control the epidemic but are accompanied by socioeconomic consequences, so the government response, community mobility, and daily confirmed cases were analyzed to determine how these policies and resulting community mobility were correlated with new cases.

Daily confirmed cases were extracted from February 15, 2020 to January 20, 2021 (1). Community mobility was extracted from Google Mobility Trends from February 15, 2020 to January 20, 2021. Google Mobility Trends records changes in the mobility of residents visiting the following six categories when compared to baseline: supermarket and pharmacy (including supermarkets, food warehouses, farmers markets, specialty food shops, and pharmacies); residential; workplaces; parks (national parks, public beaches, marinas, dog parks, plazas, and public gardens); public transport (transport hubs such as the subway/metro trains, buses, and other train stations); and retail and recreation (restaurants, cafes, shopping centers, theme parks, museums, libraries, and cinemas). Baseline was set as the mean value of mobility from January 3 to February 6, 2020, and location data for users were sampled every day to obtain percentage change from baseline. Higher mobility changes for the residential category indicated that citizens left home less often, which was aligned with epidemic control measures (4).

Government response was measured using the Oxford COVID-19 Government Response Tracker (OxCGRT) from February 15, 2020 to January 20, 2021 from Oxford University. The tracker used 19 indicators, of which the following 9 (called Stringency Index) were used in this study: school closing, cancel public events, restrictions on gatherings, close public transport, public information campaigns, restrictions on internal movement, workplace closing, stay at home requirements, and international travel controls. The index was measured on a scale of 0–100, and a higher value indicated stricter control (5).

The number of daily new cases, the OxCGRT index and the 7-day moving average value of changes in mobility according to Google are shown in Figure 1. The epidemic in Hong Kong has experienced several fluctuations. The policy adjustment is lagging behind the change of daily new cases, and the longer the lag time, the more difficult the epidemic control will be.
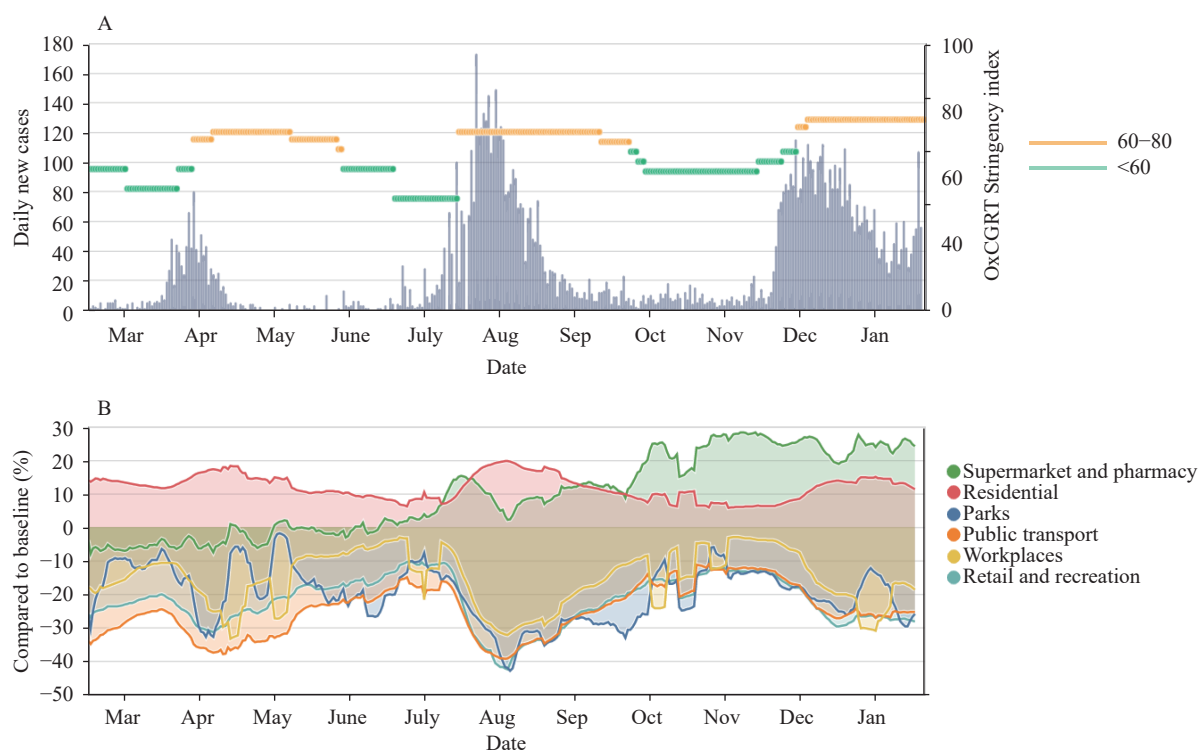
FIGURE 1. Description of the COVID-19 epidemic in Hong Kong from February 15, 2020 to January 20, 2021. (A) Daily new cases and the oxford COVID-19 government response tracker (OxCGRT). (B) Google COVID-19 community mobility (7-day moving average) compared to baseline(%).
Notes: In Figure 1A, the yellow horizontal bars represent an OxCGRT index of 60–80 and the green bars indicate a value below 60, which is relatively loose. In general, as the number of daily new cases increases, the government will respond by tightening control measures (OxCGRT increases), resulting in decreases in daily new cases.

From the outbreak in December 2020, the policy is very strict, four indicators such as parks, retail and recreation, public transport and workplaces were decreased but not as good as the outbreak in August, and people's frequency of going out to supermarket and pharmacy is still at a relatively high level, which led to the long duration of this epidemic. Since OxGRT index doesn't change frequently, the correlation analysis between daily new cases and Google Mobility Trends is taken in order to assess the impact of population mobility on epidemic.

Due to the lag between the changes in mobility and the number of daily new cases, rank correlation analysis was used to obtain the number of lag days and correlation coefficients with the strongest correlation between each indicator and the number of daily new cases (6). Among the six indicators of Google Mobility Trends, residential mobility being positively correlated with daily new cases indicated a high degree of compliance, where as the other five indicators being negatively correlated with daily new cases indicated a high degree of compliance. All statistical analyses were conducted by R statistical software(version 4.0.3; The

R Foundation for Statistical Computing, Vienna, Austria).

The results of rank correlation analysis showed that the lag days with the strongest correlation between the 6 indicators and the number of new cases per day ranged from 1 to 14 days. The supermarket and pharmacy category was positively correlated with the number of new cases per day, $r=0.351$ ($P<0.001$). The residential category was positively correlated with the number of new cases per day, $r=0.487$ ($P<0.001$). The other categories of retail and recreation, workplaces, parks, and public transport were negatively correlated with the number of new cases per day, the r values were -0.620, -0.604, -0.544, and -0.392, respectively, and P values were all less than 0.001. Among them, retail and recreation and workplaces were strongly correlated with the number of new cases per day; they both were higher than 0.6 (Table 1). Statistical significance was attributed to p values ($P<0.001$).

DISCUSSION

The speed of the epidemic may be related to many

TABLE 1. The lag days and correlation analysis of the six indicators of Google Mobility Trends relative to the number of daily new cases of COVID-19.

The categories of Google Mobility Trends	Lag days	r	P
Supermarket and pharmacy	1	0.351	<0.001
Residential	14	0.487	<0.001
Retail and recreation	14	−0.620	<0.001
Workplace	14	−0.604	<0.001
Park	11	−0.544	<0.001
Public transport	14	−0.392	<0.001

factors, such as virus variants, the number of super spreaders, etc. However, mobility restrictions and control measures can provide important information for the possibility of accelerated transmission. Analysis of daily new cases, Hong Kong Mobility Trends, and OxCGRT found that when the number of new cases increased, the government promptly tightened the response, and the Google Mobility Trends reflected that when residents had a high degree of compliance, the epidemic was well controlled. Delays in policy implementation and compliance will make the epidemic much harder to control. Overall, the population's compliance with the control policy in Hong Kong is very good in the whole year.

The last COVID-19 epidemic in Hong Kong is still going on and rebound slightly, which may be due to higher mobility comparing with the previous epidemic. Based on this situation, more protection in public, expanding testing and strict contact tracing still needs to be strengthened. Social distancing policies need to be strictly implemented among citizens, especially mask wearing and restrictions on gatherings.

Government should evaluate the six indicators of the Google Mobility Trends, especially supermarket and pharmacy, to isolate the purpose behind mobility of residents and to propose targeted solutions. Combing the relationship between the daily number of new confirmed cases, changes in mobility, and the OxCGRT for comparative analysis, researchers can predict the trends of the epidemic, choose proper times and intensities for tightening policies, and collect evidence to more precisely control the epidemic in the future. The results of the correlation analysis of daily new cases and changes in mobility concluded that the two categories of retail and recreation and workplaces were strongly correlated with the number of daily new cases, which indicates that these two venue categories should be targeted in effective epidemic control.

Although Hong Kong has relatively ample medical resources, significant increases in critical and severe cases will put tremendous pressure on the finite capacity of hospital beds. Based on the high population density, it is recommended that the government establish a list of household material reserves; regulate certain types of emergency supplies, emergency tools, and emergency medicines; and carry out targeted expansion of reserves.

Virus variants also became prevalent in some countries in mid-December 2020. In the meanwhile, the government has approved a COVID-19 vaccine that meets safety and efficacy for emergency use and has ordered 22.5 million doses. Strict testing should be continued for international students returning to Hong Kong to prevent the import of virus variants, strengthen quarantine hotel management, and avoid cross-infection.

This article didn't take into account of the virus mutation, climate factors which may also lead to the rapid increase of the cases. The OxCGRT Stringency Index of control measures were not integrated into the correlated model directly, which was lack of the assessment of control policy.

Conflicts of Interest: No conflicts of interest were reported.

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REFERENCES

1. The Government of the Hong Kong Special Administrative Region. Latest local situation of COVID-19. https://www.coronavirus.gov.hk/eng/index.html#What_is_COVID-19. [2021-1-20].
2. The Government of the Hong Kong Special Administrative Region. Statistics on testing for COVID-19 in Hong Kong. https://www.coronavirus.gov.hk/eng/index.html#What_is_COVID-19. [2021-1-20].
3. The Government of the Hong Kong Special Administrative Region. Situation on public hospitals and confirmed cases. https://www.coronavirus.gov.hk/eng/index.html#What_is_COVID-19. [2020-12-24].
4. Google. COVID-19 Community Mobility Reports. https://www.google.com/covid19/mobility/. [2021-01-20].
5. Oxford University. COVID-19 Government Response Tracker (OxCGRT). [2021-01-21]. https://www.bsg.ox.ac.uk/research/research-projects/coronavirus-government-response-tracker.
6. Chan BKC. Data analysis using R programming. In: Biostatistics for human genetic epidemiology. Cham: Springer. 2018. http://dx.doi.org/10.1007/978-3-319-93791-5_2.

Outbreak Reports

COVID-19 Cases Spread Through the K350 Train — Jilin and Heilongjiang Provinces, China, January 2021

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As of 16∶00 on January 13, 2021, 95 positive cases of coronavirus disease 2019 (COVID-19) were reported in Suihua City of Heilongjiang Province and an additional 35 cases have been linked across 7 cities in 3 provinces: Qiqihar City (7 cases), Mudanjiang City (4 cases), Harbin City (3 cases), and Yichun City (1 case) of Heilongjiang Province; Changchun City (9 cases) and Tonghua City (6 cases) of Jilin Province; and Weihai City of Shandong Province (1 case).

On January 10, 2021, the first asymptomatic infections in Changchun City of Jilin Province were found in couple recently traveling from Suihua City on January 5 (Suihua A and B; 58-year-old male and 57-year-old female, respectively). After hearing of the outbreak in Suihua City, the couple voluntarily sought testing at the Second Hospital of Jilin University and returned positive COVID-19 tests. The initial investigation of the couple patients indicated that they had traveled from Suihua City to Changchun by the K350 Train on January 5. This launched an epidemiological investigation of close contacts and for other passengers of the K350 train on January 5.

INVESTIGATION AND FINDINGS

On January 11, 2021, close contact tracing found that the son of Suihua A and B had tested positive for COVID-19. On January 12, nucleic acid screening of the K350 train found 3 more asymptomatic infections in passengers: 2 residing in Changchun City (Changchun A and B; 53-year-old male and 48-year-old female, respectively) and 1 residing in Tonghua City (Tonghua A; 44-year-old male). These 5 patients all rode in the same passenger car of the K350 train and were in relatively close proximity as shown in Figure 1. Another 4 asymptomatic infections were detected in close contacts of Tonghua A, which resulted in a total of 10 infections linked to K350 in Jilin Province as of January 13. Table 1 shows a partial timetable of the times Suihua A and B, Changchun A

and B, and Tonghua A were found to be aboard K350 together.

Suihua A and B were likely infected while visiting relatives in Suihua and began experiencing symptoms on January 3, which subsided by the time they were tested on January 10. The couple boarded the K2209 train on December 28, 2020 and arrived in Suileng County of Suihua at 05∶00 on December 29. They attended a large gathering for dinner involving approximately 20 people including the father of the index patient of Wangkui County of Suihua who became ill on January 3, 2021 and was diagnosed on January 10. On December 30, 2020, Suihua A and B attended a wedding involving approximately 190 people and then had dinner at Suihua A's uncle's home, at which Suihua A's younger brother (Qiqihar City's index patient; experienced symptoms from January 6 to 9 and was diagnosed on January 12) and younger sister (Yichun City's index patient; voluntarily sought testing and was diagnosed on January 11). On January 3, Suihua A and B began experiencing symptoms of dizziness and drowsiness; they made a warm ginger drink but did not seek medical care.

Suihua A and B boarded K350 at roughly 14∶30 from Suihua Station and alighted at 20∶00 at Changchun Station. Changchun A and B boarded K350 at roughly 16∶30 from Harbin West Station of Heilongjiang Province and alighted at 20∶00 at Changchun Station. Tonghua A boarded K350 at roughly 11∶20 from Nancha Station in Heilongjiang Province and alighted at 16∶30 at Harbin West Station. However, Tonghua A took additional trains after completing his journey from January 7 to 9 including Z174, K1383, and D124. Further investigations are being conducted.

Tonghua A conducted a work training seminar from January 10 to 11, 2021 in Tonghua City. After Tonghua A was confirmed to be COVID-19 positive, 4 asymptomatic infections were found among attendees of the training seminar.
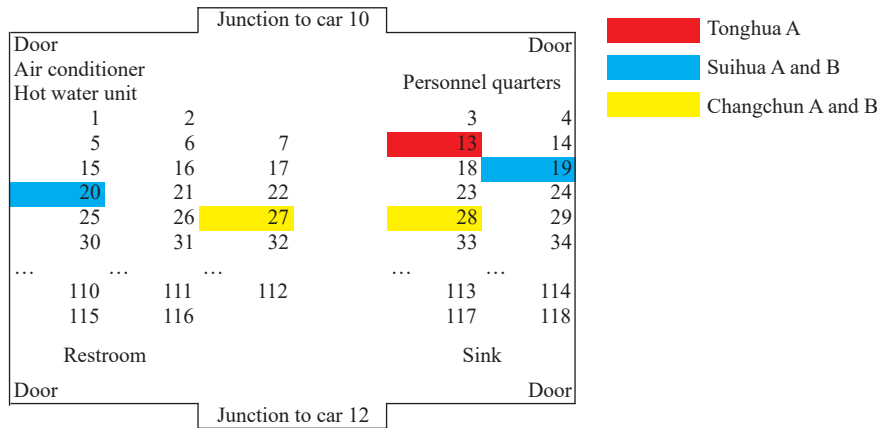
FIGURE 1. A diagram of where the patients in this outbreak were seated in Car 11 of the K350 train that departs daily from Jiamusi Station at 09：28 and arrives in Beijing at 13：00 the next day.
K350 passes through 18 stations across 4 provinces (Heilongjiang, Jilin, Liaoning, and Hebei) and 2 municipalities (Tianjin and Beijing). The total journey time is approximately 27 hours and 32 minutes.

TABLE 1. A diagram showing the overlap of patients found in this outbreak.

Station #	Station name	Arrival time	Departure time	Standby length (minutes)	Tonghua A	Suihua A&B	Changchun A&B
1	Jiamusi	9:28	9:28	–			
2	Nancha	11:22	11:25	3			
3	Langxiang	12:04	12:06	2			
4	Tieli	13:09	13:11	2			
5	Suihua	14:33	14:41	8			
6	Harbin West	16:28	17:00	32			
7	Shuangchengbao	17:33	17:36	3			
8	Dehui	18:44	18:46	2			
9	Changchun	19:42	20:05	23			
10	Gongzhuling	20:43	20:45	2			

Note: Patients Suihua A and B (blue) were likely the source of COVID-19 and likely transmitted the infection to Tonghua A (red) and Changchun A and B (yellow).

DISCUSSION

The linkage of cases in this outbreak of COVID-19 across several cities and provinces in northern China suggests that current measures must be diligently maintained and citizens must closely follow guidelines and promptly seek testing when they suspect they have symptoms. Though the K350 train is air conditioned, the cold winter conditions lead to worse ventilation and can lead to periods of extended exposure if a source of infection is close by.

As the Spring Festival (Lunar New Year) approaches, a period of extensive travel across China will commence as residents return home to their families, and existing prevention and control measures will be tested. A high potential of superspreading events and of outbreaks spanning entire regions exists, and to prevent extended periods of lockdown like that most recently occurring in Hebei Province (1), one of the strongest measures in the public health arsenal of non-pharmaceutical interventions, all stakeholders must buy in.

Current measures include the following: 1) passengers boarding from low-risk areas should provide negative nucleic acid test results within the most recent seven days; 2) medium to high-risk areas will have ticket purchases suspended, passengers will be prevented from boarding, and purchased tickets will be refunded online; 3) passengers will be given basic health precaution training including advocating strict mask wearing, proper hand hygiene, and supervision of these measures by train staff; and 4) railway operating companies will register passenger information, increase monitoring and enforcement of public health

measures, and promptly report any abnormalities.

Despite careful measures reducing the inflow of individuals coming into China, the new variants of COVID-19 have been reported in China already including the VUI202012/01 variant first emerging in the United Kingdom (*2*) and the 501Y.V2 variant first emerging in South Africa (*3*). In addition, COVID-19 has been shown to spread via frozen food products and related packaging (*4*), which was not established at the beginning of the pandemic. All these events indicate the process of understanding and combatting a new virus threat, and how in order to reduce the disease burden on the population, all aspects of the response, including policymakers, implementers, and the public, must contribute equally while the measures can be developed, fine-tuned, and perfected.

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REFERENCES

1. Qi SX, Zhao X, Hao P, Liu NK, Gao GF, Song Y, et al. Two reemergent cases of COVID-19 — Hebei Province, China, January 2, 2021. China CDC Wkly 2021;3(2):25 – 7. http://dx.doi.org/10.46234/ccdcw2021.006.
2. Chen HY, Huang XY, Zhao Z, Song Y, Hao P, Jiang H, et al. The first case of new variant COVID-19 originating in the United Kingdom detected in a returning student — Shanghai Municipality, China, December 14, 2020. China CDC Wkly 2021;3(1):1 – 3. http://dx.doi.org/10.46234/ccdcw2020.270.
3. Chen FJ, Li BS, Hao P, Song Y, Xu WB, Liu NK, et al. A case of new variant COVID-19 first emerging in South Africa detected in airplane pilot — Guangdong Province, China, January 6, 2021. China CDC Wkly 2021;3(2):28 – 9. http://dx.doi.org/10.46234/ccdcw2021.007.
4. Bai L, Wang YR, Wang YBN, Wu YN, Li N, Liu ZP. Controlling COVID-19 transmission due to contaminated imported frozen food and food packaging. China CDC Wkly 2021;3(2):30 – 3. http://dx.doi.org/10.46234/ccdcw2021.008.

Methods and Applications

Bibliometric Analysis on Utilization of New Information Technology in the Prevention and Control of COVID-19 — China, 2020

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ABSTRACT

Introduction: New information technology (IT) has been applied to prevent and control coronavirus disease 2019 (COVID-19) in many regions of China since the outbreak of COVID-19. This study aims to illustrate the current status and key areas of the application of new IT in the prevention and control of COVID-19.

Methods: Literature related to the prevention and control of COVID-19 with new IT since 2020 was retrieved from China National Knowledge Internet and Wanfang Literature databases, the two most authoritative databases in China. CiteSpace 5.7.R2 was used to analyze the institutions, authors, and keywords of the articles. The application of new IT is determined by keywords and highly cited documents.

Results: A total of 1,711 articles were included, as the number of publications has been continually increasing over the investigation period. The six hot topics of new IT applied in COVID-19 were big data, artificial intelligence, Internet+, blockchain, Internet of Things, and 5G. The most productive institution is University of Chinese Academy of Sciences, and the most productive author in this field is Tao Pei, whose article, "Multi-level Spatial Distribution Estimation Model of the Inter-Regional Migrant Population Using Multi-Source Spatio-Temporal Big Data: A Case Study of Migrants from Wuhan During the Spread of COVID-19," was highly cited.

Discussion: This study could help medical professionals understand the application status and research trends of new IT in the prevention and control of COVID-19. This paper also helps researchers find potential co-operative institutions and partners.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) has caused more than 70 million reported cases and more than 1 million deaths worldwide since emerging at the end of 2019, causing huge human capital loss and material and financial losses in 2020. A series of traditional infectious disease prevention and control measures, including wearing masks, going out less frequently, washing hands, and social distancing were taken to control COVID-19 (1).

Unlike past infectious diseases, COVID-19 is currently the only large-scale epidemic that humankind has encountered in the era of big data. More importantly, many new information technologies (ITs) have been used to help to control the epidemic. According to experts, the new generation of information technology, includes big data, artificial intelligence (AI), 5G, Internet of Things (IOT), blockchain, and other technologies (2). In this article, new IT is confined to AI, big data, blockchain, 5G, internet, cloud computing, IOT, robotics, bluetooth, and knowledge graphs. This study explores and summarizes the new IT's current role in responding to COVID-19.

METHODS

Data Acquisition

The literature data used in this study were retrieved and downloaded from the China National Knowledge Internet (CNKI) and Wanfang Literature databases. The publication date was defined as "after 2020", and the literature type was defined as "article." By searching [topic: (AI or big data or blockchain or 5G or internet or cloud computing or IOT or robotics or Bluetooth or data modeling or internet public opinion or Search Engine or knowledge graphs) and topic: (COVID-19 or NCP*)] and Date: 2020-* (searching date: December 24, 2020) as well as removing duplicate and off-topic literature and excluding review and report

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* NCP: novel coronavirus pneumonia.

papers, a total of 4,621 articles were retrieved, of which 1,711 references were included in this study. At the same time, all papers were screened by experts, and controversial documents were further discussed to decide their eligibility.

Analysis Tool

This study used Citespace5.7.R2 software for bibliometric analysis, as it highlighted the keywords, authors, institutions, and other information of the literature and generated visual knowledge maps composed of nodes and links. Each node in a map represents an element, such as institution, author, and keyword, and the size of the node is proportional to the frequency with which the selected node type occurs. The number of connections and the strength of links between nodes represented relationships of collaboration or co-citations between nodes, and the number is in direct proportion to the degree of connection. The centrality of a node referred to the number of any shortest paths through this point in its network and was a measure of the connecting role played by a node in the overall network. Nodes with centrality ≥0.1 were called critical nodes. Network density represented the density of the network generating knowledge graph. The different colors of nodes and lines represented different publication years (3).

The parameters of CiteSpace were defined as follows: time slicing (2020–2021), years per slice (1), term source (all selection), node type (choose one at a time), selection criteria (top 50%), and pruning (pathfinder).

RESULTS

Analysis of the Institutions

Taking "institution" as the node type, the map produced 316 nodes and 181 links. In total, 1,711 articles came from 316 institutions. The top five institutions that produced the most articles were: University of Chinese Academy of Sciences; School of Architecture, Tsinghua University; Institute of Geographic Sciences and Natural Resources Research, University of Chinese Academy of Sciences; China Academy of Information and Communications Technology; School of Information Management, Wuhan University. There were some collaborations between these institutions. However, the centrality of

the collaborations was 0, indicating that the collaboration among research institutions was insignificant.

Analysis of the Authors

Taking "author" as the node type, the map produced 212 nodes and 386 links. The 1,711 articles were written by 212 authors. Removing the influence of the same name, the top five authors are Tao Pei, Ci Song, Xiaoxiang Zhang, Ying Long, and Chenghu Zhou.

These authors are regarded as active researchers in the area. References with high citation frequency by active authors can be regarded as hot topics in the research field. The most highly cited article among his publications on COVID-19 prevention and control is "Multi-level Spatial Distribution Estimation Model of the Inter-Regional Migrant Population Using Multi-Source Spatio-Temporal Big Data: A Case Study of Migrants from Wuhan During the Spread of COVID-19," published in the *Journal of Geo-Information Science*, focusing on the estimation of the spatial distribution of the displaced population in Wuhan based on big data (4). This paper showed that big data can quickly respond to public health emergencies and provide scientific numeric support for decision-making. There were some collaborations among authors, but the centrality of the collaborations was 0, indicating insignificant collaboration among authors.

Analysis of Keyword Cooccurrence

Taking "term" and "keyword" as the network nodes, after combining synonyms and deleting of meaningless keywords, the generated keyword knowledge map contains 179 nodes, 299 links, and a network density of 0.0188 (Figure 1). The top 20 keywords and their frequency centrality are shown in Table 1.

The frequency of keywords showed that the application of new IT in the prevention and control of COVID-19 mainly focused on big data, artificial intelligence, internet, blockchain, IOT, and 5G. It was mainly used in public opinion monitoring, online teaching, telemedical system, emergency management, outbreak prediction, and epidemic information visualization. The details of six hot topics about new IT were as follow:

1) Big data

As shown in Figure 1 and Table 1, the most often used new IT was big data. Big data were applied in the
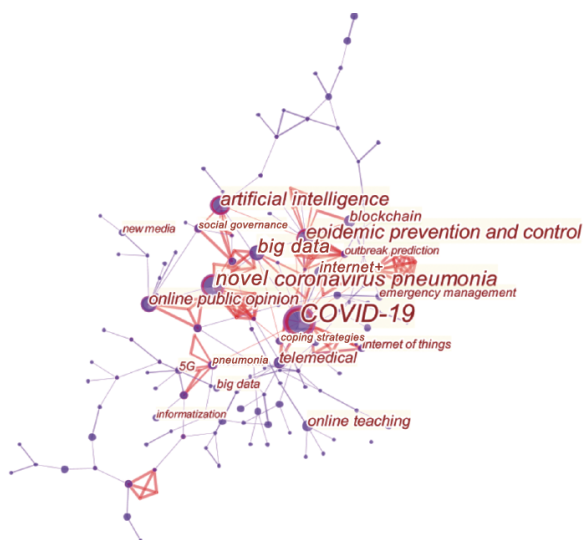
FIGURE 1. Co-occurrence of 179 keywords related to the application of new information technologies to the COVID-19. Each dot in the graph represents a keyword, and the lines indicate the relationship between the keywords. It was evident that the new information technologies in the prevention and control of the COVID-19 epidemic were large and interconnected.

analysis of online public opinion, population movement, close contacts investigation, timely acquisition of epidemic information, and the estimation of the spread of information (5).

2) AI

AI combined with computed tomography (CT) were used to assist doctors in diagnostics. AI was also combined with big data to improve the epidemic prediction model, as well as being combined with robotics to perform ward management (6).

3) Internet Plus (Internet+)

Thanks to Internet+, telemedical and online teaching were also in the top 20 co-occurring keywords. In order to reduce the flow of people and decrease in-person transits, educational institutions adopted online teaching through the slogan of "No In-Person Teaching, No Suspension of Studying". Most colleges and universities relied on the internet to carry out online teaching in the form of live or recorded broadcasting (7). In the medical field, many public hospitals opened internet diagnosis and treatment services, such as fever clinics and COVID-19 symptoms consultations, to re-allocate medical resources, optimizing the usage of medical resources (8).

4) Blockchain

Blockchain was mainly used for emergency material

TABLE 1. The top 20 keywords about the application of new information technology to prevention and control of COVID-19, December 24, 2020.

Number	Frequency	Centrality	Key words
1	613	0.76	Coronavirus Disease 2019 (COVID-19)
2	239	0.43	Novel coronavirus pneumonia
3	148	0.35	Epidemic prevention and control
4	119	0.31	Big data
5	107	0.46	Artificial intelligence
6	54	0.01	Internet+
7	49	0.27	Online public opinion
8	45	0.06	Online teaching
9	38	0.12	Telemedical
10	26	0.08	Blockchain
11	18	0.02	Internet of things
12	18	0.04	5G
13	17	0.06	Emergency management
14	17	0.02	Outbreak prediction
15	14	0.02	New media
16	13	0.10	Social governance
17	12	0.43	Coping strategies
18	12	0	Informatization
19	12	0.29	Pneumonia
20	12	0.06	Epidemic information visualization

supply management in COVID-19 prevention and control. Blockchain could provide anti-counterfeiting and traceable services for rescue materials. The materials embedded with blockchain technology assisted in keeping accurate transportation records, which effectively promoted information exchange and resource coordination during the process of material allocation. Blockchain could also be coordinated with technologies like artificial intelligence, health codes, IOT, and private chains to investigate close contacts (*9*).

5) IOT

The IOT was combined with artificial intelligence and blockchain for auxiliary diagnosis and treatment, the delivery of rescue materials, and management of community residents (*10*).

6) 5G

In the COVID-19 epidemic, 5G provided network infrastructure for square-cabin (Fangcang Shelter) hospitals, Huoshenshan Hospital, and Leishenshan Hospital. It also provided network support for the hospitals' telemedicine and robots, and other information facilities (*11*).

DISCUSSION

Based on the bibliometric analysis of new IT in the Prevention and Control of COVID-19 publications in China 2020, the amount of relevant literature has been bountiful. The phenomenon of cooperation among multiple authors is widespread in this research field. Almost all highly cited articles were completed by more than one author. However, cooperation among institutions was not as wide.

This research suggested that many new information technologies played important roles in various aspects of COVID-19 prevention and control. They were used either with other new ITs or with traditional industries.

Big data was used most widely in the process of COVID-19 prevention and control among all new information technologies. It was especially common in the investigation of close contacts, during which it largely supplements traditional epidemiological investigations. The combination of artificial intelligence technology and lung CT examination technology enabled doctors to make diagnoses much faster. In addition, 5G technology was quickly built in square-cabin (Fangcang shelter) hospitals, Huoshenshan Hospital, and Leishenshan Hospital due

to its high broadband, low latency, and wide connection advantages. The information system and wireless network were fully covered to help Wuhan Hospital's COVID-19 prevention and control. The Internet of Things and blockchain were combined with big data and artificial intelligence technology to construct personal health codes and deliver of rescue materials.

At the same time, under the circumstance that many local cases caused by frozen imported products, it is recommended that we establish a blockchain-enabled tracing system for imported frozen products based on the safety and traceability characteristics of blockchain. Accordingly, virus tracing and COVID-19 control can be carried out as soon as possible after local cases occur. In terms of medical care, many hospitals relied on internet technology to open online consultation services, and patients could go to fever clinics online for consultation about COVID-19 symptoms. In terms of education, from elementary schools to universities, educational institutions could continue online teaching in the form of live broadcast or recording.

This study was subject to some limitations. First, the literature data of this study came from CNKI and Wanfang Literature databases, so domestic experts' papers published in foreign journals were not included in this study. Second, this study only focused on literature with high citation frequency at the present stage, and a bias may exist in the results of study analysis and the actual status of the studies because more recent papers will have fewer times cited. Finally, all papers were retrieved on November 30, 2020, and the literature after that was not included.

In conclusion, this study could help medical professionals understand the application status and trends of new IT in the prevention and control of COVID-19 and help researchers find cooperative institutions and partners.

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REFERENCES

1. National Health Commission. Prevention and control plan of COVID-19 (7th edition). Chin J Infect Control 2020;19(11):1042 – 8. http://dx.doi.org/10.12138/j.issn.1671-9638.20206164. (In Chinese).

2. The State Council of the People's Republic of China. "The decision on speeding up the cultivation and development of strategic emerging industries" was issued by the State Council. http://www.scio.gov.cn/xwfbh/xwbfbh/wqfbh/2012/0608/xgzc/Document/961711/961711.htm. [2010-10-27]. (In Chinese).

3. Chen CM. Science mapping: a systematic review of the literature. J Data Inf Sci 2017;2(2):1 – 40. http://dx.doi.org/10.1515/jdis-2017-0006.

4. Liu Z, Qian JL, Du YY, Wang N, Yi JW, Sun YR, et al. Multi-level spatial distribution estimation model of the inter-regional migrant population using multi-source spatio-temporal big data: a case study of migrants from Wuhan during the spread of COVID-19. J Geo-Inf Sci 2020;22(2):147 – 60. http://dx.doi.org/10.12082/dqxkx.2020.200045. (In Chinese).

5. Zhao XM, Li XH, Nie CH. Backtracking transmission of COVID-19 in China based on big data source, and effect of strict pandemic control policy. Bull Chin Acad Sci 2020;35(3):248 – 55. http://dx.doi.org/10.16418/j.issn.1000-3045.20200210002. (In Chinese).

6. Lyu ZB, Guan CS, Yan S, Chen QY, Li JJ, Zhang YJ, et al. Value of CT findings in predicting transformation of clinical types of COVID-19. J Cap Med Univ 2020;41(3):340 – 4. http://dx.doi.org/10.3969/j.issn.1006-7795.2020.03.004. (In Chinese).

7. Feng W, Zhang LN, Li JY, Wei T, Peng TT, Zhang DX, et al. Analysis of special ehealth service for corona virus disease 2019 (COVID-19) pneumonia. J Peking Univ (Health Sci) 2020;52(2):302 – 7. http://dx.doi.org/10.19723/j.issn.1671-167X.2020.02.018. (In Chinese).

8. Wu DG. The retrospect and reflection of educational technology evolution: online teaching in universities under the epidemic situation. China High Educ Res 2020(4):1 – 6, 11. http://dx.doi.org/10.16298/j.cnki.1004-3667.2020.04.01. (In Chinese).

9. Hu QH, He J, Dong Q. Research on emergency materials supply information management of medical epidemic prevention under blockchain architecture——targeted donation of COVID-19 prevention materials as an example. Health Econ Res 2020;37(4): 10-4. https://kns.cnki.net/kcms/detail/detail.aspx?dbcode=CJFD&dbnameCJFDLAST2020&filenam=WSJJ202004004&v0dzPaFRyijo5ruSAuQAsCOF%25mmd2BJ9Hl57%25mmd2BrT8gBvmVjvnLVsUDYxJZ06zoTlclPgp7J. [2021-1-15] (In Chinese).

10. Bai L, Yang DW, Wang X, Tong L, Bai CX, Zhong NS. Chinese experts consensus on the Internet of Things-aided diagnosis and treatment of COVID-19. Fudan Univ J Med Sci 2020;47(2):151 – 60. http://dx.doi.org/10.3969/j.issn.1672-8467.2020.02.002. (In Chinese).

11. Zhou B, Wu Q, Zhao XF, Zhang WC, Wu WJ. Practice of cabin hospital network and information system based on 5G all wireless technology. China Digit Med 2020;15(5):5 – 7. http://dx.doi.org/10.3969/j.issn.1673-7571.2020.05.002. (In Chinese).

Methods and Applications

Determining the Covertness of COVID-19
— Wuhan, China, 2020

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ABSTRACT

Introduction: The coronavirus disease 2019 (COVID-19) pandemic has been going on for over a year and has reemerged in several regions. Therefore, understanding the covertness of COVID-19 is critical to more precisely estimating the pandemic size, especially the population of hidden carriers (those with very mild or no symptoms).

Methods: A stochastic dynamic model was proposed to capture the transmission mechanism of COVID-19 and to depict the covertness of COVID-19. The proposed model captured unique features of COVID-19, changes in the diagnosis criteria, and escalating containment measures.

Results: The model estimated that, for the epidemic in Wuhan, 79.8% (76.7%–82.7%) of the spread was caused by hidden carriers. The overall lab-confirmation rate in Wuhan up until March 8, 2020 was 0.17 (0.15–0.19). The diagnostic rate among patients with significant symptoms went up to 0.82 on March 8, 2020 from 0.43 on January 1, 2020 with escalating containment measures and nationwide medical supports. The probability of resurgence could be as high as 0.72 if containment measures were lifted after zero new reported (lab-confirmed or clinically confirmed) cases in a consecutive period of 14 days. This probability went down to 0.18 and 0.01 for measures lifted after 30 and 60 days, respectively.

Discussion: Consistent with the cases detected in Wuhan in mid-May, 2020, this study suggests that much of the COVID-19 pandemic is underreported and highly covert, which suggests that strict measures must be enforced continuously to contain the spread of the pandemic.

INTRODUCTION

The outbreak of coronavirus disease 2019 (COVID-19) has been going on for over a year and has been deemed as a once-in-a-century health crisis (*1*). Many countries that believed they had gone through the worst are now again grappling with new outbreaks (*1*). A major driving force in the persistence of COVID-19 is transmission caused by hidden carriers with very mild or no symptoms who are unaware of their infection (*2*). Due to the covertness of COVID-19 and overburdened medical resources, low diagnostic rates have been observed globally. The number of infected cases estimated by seroprevalence in various regions of the US were 6 to 24 times higher than the reported number (*3*). Therefore, understanding the covertness of COVID-19 is critical to getting a more precise picture of the pandemic size, especially the population of hidden carriers, and accordingly, making public health decisions such as the timing to lift containment measures.

Previous studies have unraveled the covert features of COVID-19, including incubation period, proportion and transmissibility of asymptomatic infections (*4–7*), and overall reporting rates (*7–8*). Hao et al. (2020) provided an important perspective on the transmission dynamics of COVID-19 in Wuhan. The key finding inferred that 87% of the infections before March 8, 2020 were not lab-confirmed (note that a lab-confirmed case is defined as a case who is symptomatic and tested positive for COVID-19; clinically-confirmed cases and detected asymptomatic cases were excluded) (*8*). However, due to limitations such as violation of the homogeneity assumption in compartment dynamic models, flawed inference of transmissibility parameters, and the inability to distinguish the covert nature of COVID-19 from external factors (i.e., overburdened medical recourses), the study failed to capture some important information of covertness which led to an overoptimistic estimate on the all-clearance date in Wuhan (see Supplementary Material Appendix A for details, available in http://weekly.chinacdc.cn/).

In this paper, inspired by the SAPHIRE model in Hao et al. (2020), an improved dynamic model was proposed to depict the covertness of COVID-19 to gain a better understanding of the diagnostic rate and the probability of resurgence under different policies.

METHODS

The proposed model included 6 compartments: susceptible (S), exposed (E), presymptomatic infectious (P), infectious with significant symptoms (I), infectious without significant symptoms (A), and removed (R). The individuals in I had significant symptoms that would be diagnosable but might not be lab-confirmed. For example, when the medical system was seriously overburdened, even a severe symptomatic case might not be diagnosed or hospitalized promptly before the viral load had dropped to the level that the infection could no longer be detected by tests. Meanwhile, compartment A included hidden carriers who were unlikely to be detected. Therefore, compared to the original SAPHIRE model, individuals in A or I would now show better homogeneity, which was a required underlying assumption in compartmental dynamic models. Individuals in A could only transit to R by losing transmissibility pathologically, while patients in I might reach R either by losing their transmissibility pathologically or by isolation upon lab-confirmation or clinical diagnosis. The transmission rate was set to vary over different time periods based on the local social events, medical resources, and implementation of containment measures. The covertness of COVID-19 can be better understood by dividing the diagnostic rate (hereafter referred to as lab-confirmation rate) into the following two components:

1) the natural characteristics of COVID-19 on covertness, i.e. the fraction of those infectious virus carriers without significant symptoms throughout their course of disease;

2) factors related to medical resources and containment measures, which could be replenished and help improve the diagnostic rate in the later stages of the outbreak.

In the proposed model, these components were estimated separately. In addition, in reality, transmissibility decreased towards the end of the infectious period (9), hence, the assumption of a constant transmission rate throughout compartment I and A might potentially lead to an overestimation of effective reproduction number R_e in the early stages. The proposed model had also taken these issues into consideration (see Appendix B for the solution details and ODE system description, available in http://weekly.chinacdc.cn/).

RESULTS

The same data from January 1 to February 29 from Wuhan in Hao et al. (2020) were used here for comparison. A total of 5 time periods were identified as in Hao et al. (2020) in Wuhan for the transmission rate to vary. Based on the stochastic dynamic model, the effective reproduction R_e in Wuhan was 4.49 (4.01–5.00) and 4.10 (3.71–4.52), respectively, in the first 2 periods of January 1–9 (before *Chunyun*, the period of intense travel preceding the Spring Festival) and January 10–22 (*Chunyun*), then dropped dramatically to 1.00 (0.92–1.07), 0.43 (0.40–0.46), and 0.27 (0.22–0.33) in the later 3 periods (Figure 1B). These implied that the pandemic had been preliminarily controlled since the third period. It was estimated that 79.8% (76.7%–82.7%) of the spread of the disease was caused by hidden carriers (namely population in A and P). The estimated cumulative number of infections up until March 8 was 194,302 (170,190–220,691) and the overall lab-confirmation rate was 0.17 (0.15–0.19), which was of a similar order as in Hao et al (2020).

However, such a low lab-confirmation rate was mostly caused by the high proportion of asymptomatic or very mild cases which was estimated to be 0.74 (0.71–0.77), while the diagnostic rate among patients with significant symptoms (namely patients in I) went up to 0.82 on March 8 from 0.43 on January 1 because of the escalating containment measures and nationwide medical support (Figure 1C). This estimation indicated that most of those with significant symptoms in Wuhan would be promptly diagnosed in the later stage of the outbreak. The clearance of all active infections would occur on June 3 (May 15 to July 5) assuming the trend remained unchanged as in the fifth period. These estimates were significantly more consistent with the confirmed cases reported in Wuhan in May, and the hidden carriers detected in subsequent city-wide testing (10). In regard to the decision making of continuous surveillance and interventions, the model found that if all measures were lifted after zero new reported (lab-confirmed or clinically-confirmed) cases in a consecutive period of 14 days, the probability of resurgence was still as high as 0.72 (Figure 1D). This probability went down to 0.18 and 0.01 if measures were lifted after zero new confirmed case in a consecutive period of 30 and 60 days, respectively. See Appendix C for more details, available in http://weekly.chinacdc.cn/.
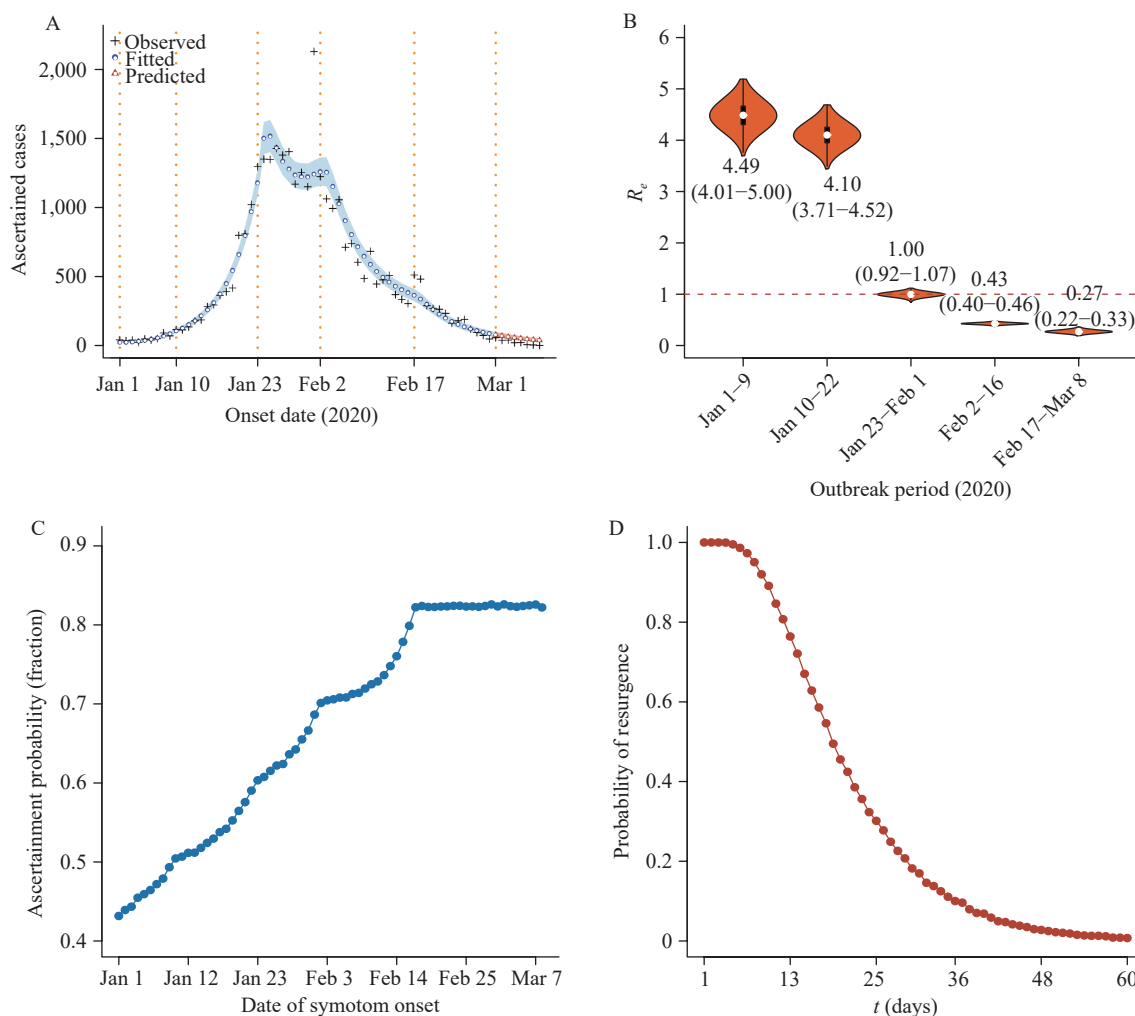
FIGURE 1. Results of primary analysis: epidemic trends, effective reproduction numbers, ascertainment probabilities, and probabilities of resurgences. (A) Fitting and prediction using parameters from the fifth period (February 17–29), the shaded area is the 95% credible intervals, and the colored points are the mean values based on 20,000 MCMC samples. (B) Distribution of R_e estimates from 20,000 MCMC samples. (C) Diagnostic rate among patients with significant symptoms. (D) Probability of resurgence if control measures were lifted after zero new lab-confirmed cases for t days consecutively.
Note: (C) the y-axis is the probability that a patient with significant symptom can be ascertained.
Abbreviation: MCMC=Markov chain Monte Carlo.

DISCUSSION

In this study, the model estimation is consistent with the number of cases detected in Wuhan in mid-May. In comparison with reproduction numbers in other published studies, the estimate in the first period is in the range but on the higher side (*11–13*). It is possibly due to most of the other published reproduction numbers being estimated for the period after first period in this study (January 9) and that earlier data were not as complete, which might lead to an overestimation in reproduction number. Furthermore, the results suggested that COVID-19 was highly covert, the spread of the disease in Wuhan was mostly caused by hidden carriers, and the probability of resurgence was high even if the measures were retained for 14 consecutive days after reaching 0 new reported cases, which may explain the resurgence in new infections over the past few months in other countries. As a result, continuous and sometimes even painstaking endeavors have to be made in order to contain the spread of the pandemic. Large-scale testing is encouraged towards the end of a significant outbreak to identify and quarantine hidden carriers before a city or nation can be safely reopened. In particular, the model implies that it takes more than 4 months in Wuhan from a strict lockdown to the final clearance of all active infections.

The model in this study can be extended to fit

pandemic data outside Wuhan, though modifications are needed with respect to specific countries or regions. For example, in the United States, statistics on daily reported cases are publicly available, but 1) no distinction is made between symptomatic and asymptomatic cases, 2) the dates of symptoms onset are mostly unavailable, 3) most reported cases are only required to self-isolate, which means that even if a case is reported, there is still a chance of infecting others. Moreover, we also need to track the changes of non-pharmaceutical interventions within the region of interest, to which (*14*) can be a helpful reference. To accommodate such differences, an additional compartment is needed for reported cases.

To conclude, the proposed model reflects the unique features of COVID-19, the changes in the diagnostic criteria, and the escalating containment measures, and hence the corresponding model estimates offer a better understanding of the diagnostic rate and the probability of resurgence under different policies. COVID-19 is highly covert, 74% (71%–77%) of the virus carriers had no/mild symptoms, 80% (77%–83%) of the spread of the disease was caused by those hidden carriers, and as a result, the probability of resurgence is high.

This study shares some limitations in Hao et al. (2020), for example, the assumption of homogeneous transmission rate within the population while ignoring heterogeneity between groups by sex, age, geographical region, socioeconomic status. Moreover, the population movement in this study is modelled under the same relatively simple setting as in Hao et al. (2020). This is acceptable for the case of Wuhan due to the travel restriction since January 23. More sophisticated modelling on travel flows is needed in order to generalize this model to other regions. Finally, the recently reported SARS-CoV-2 mutants may pose potential challenge to the generalization of the proposed model. Even when control measures remain unchanged, the emergence and spread of new COVID-19 variants may change the transmission rate and thus make the epidemic trend deviate from our prediction. These will be explored in future research when more relevant epidemiological data are available.

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REFERENCES

1. WHO. COVID-19 Emergency Committee highlights need for response efforts over long term. https://www.who.int/news/item/01-08-2020-covid-19-emergency-committee-highlights-need-for-response-efforts-over-long-term. [2020-8-1].
2. WHO. Virtual press conference on COVID-19 in the western Pacific, Remarks by Dr Takeshi Kasai. https://www.who.int/westernpacific/news/speeches/detail/virtual-press-conference-on-covid-in-the-western-pacific. [2020-8-18].
3. Havers FP, Reed C, Lim T, Montgomery JM, Klena JD, Hall AJ, et al. Seroprevalence of antibodies to SARS-CoV-2 in 10 Sites in the United States, March 23-May 12, 2020. JAMA Intern Med 2020;180(12):1576 – 86. http://dx.doi.org/10.1001/jamainternmed.2020.4130.
4. Hu ZL, Song C, Xu CJ, Jin GF, Chen YL, Xu X, et al. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. Sci China Life Sci 2020;63(5):706 – 11. http://dx.doi.org/10.1007/s11427-020-1661-4.
5. Nishiura H, Kobayashi T, Miyama T, Suzuki A, Jung SM, Hayashi K, et al. Estimation of the asymptomatic ratio of novel coronavirus infections (COVID-19). Int J Infect Dis 2020;94:154 – 5. http://dx.doi.org/10.1016/j.ijid.2020.03.020.
6. Zhang Y, You C, Cai ZH, Sun JR, Hu WJ, Zhou XH. Prediction of the COVID-19 outbreak in China based on a new stochastic dynamic model. Sci Rep 2020;10(1):21522. http://dx.doi.org/10.1038/s41598-020-76630-0.
7. Li RY, Pei S, Chen B, Song YM, Zhang T, Yang W, et al. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV-2). Science 2020;368(6490):489 – 93. http://dx.doi.org/10.1126/science.abb3221.
8. Hao XJ, Cheng SS, Wu DG, Wu TC, Lin XH, Wang CL. Reconstruction of the full transmission dynamics of COVID-19 in Wuhan. Nature 2020;584(7821):420 – 4. http://dx.doi.org/10.1038/s41586-020-2554-8.
9. Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, et al. Virological assessment of hospitalized patients with COVID-2019. Nature 2020;581(7809):465 – 9. http://dx.doi.org/10.1038/s41586-020-2196-x.
10. City-wide screening results (5 days) released in Wuhan, 58 new asymptomatic cases detected. http://www.sanyarb.com.cn/content/2020-05/20/content_495360.htm. [2020-5-20]. (In Chinese).
11. Liu Y, Gayle AA, Wilder-Smith A, Rocklöv J. The reproductive number of COVID-19 is higher compared to SARS coronavirus. J Travel Med 2020;27(2):taaa021. http://dx.doi.org/10.1093/jtm/taaa021.
12. Sanche S, Lin YT, Xu CG, Romero-Severson E, Hengartner N, Ke RA, et al. High contagiousness and rapid spread of severe acute respiratory syndrome coronavirus 2. Emerg Infect Dis 2020;26(7):1470 – 7. http://dx.doi.org/10.3201/eid2607.200282.
13. Zhao SL, Chen H. Modeling the epidemic dynamics and control of COVID-19 outbreak in China. Quant Biol 2020;8(1):11 – 9. http://dx.doi.org/10.1007/s40484-020-0199-0.
14. Hale T, Angrist N, Cameron-Blake E, Hallas L, Kira B, Majumdar S, et al. Oxford COVID-19 government response tracker. Blavatnik school of government. https://www.bsg.ox.ac.uk/research/research-projects/coronavirus-government-response-tracker. [2020-06-22].

Supplymentary Material

Appendix A: Concerns on the SAPHIRE model proposed by Hao et al. (2020) (*1*)

The SAPHIRE model included 7 compartments susceptible (*S*), exposed (*E*), presymptomatic infectious (*P*), ascertained infectious (*I*), unascertained infectious (*A*), isolation in hospital (*H*), and removed (*R*). For ease of understanding, *R* was suggested understanding as the loss of transmissibility pathologically to be distinguished from *H*. An individual in *S* would be infected by individuals in *P*, *I*, or *A* with different transmissibility to get into *E* and then *P* after a latent period. At the time point of symptoms onset, an individual transitioning from *P* to *I* or A depending on whether they would be lab-confirmed in the future, and the ascertainment rate (*r*) is the ratio that a patient would be lab-confirmed. For a case to be lab-confirmed, the patient must be both symptomatic and testing positive, which means individuals in *I* must be symptomatic, while those who were in *A* could be asymptomatic and their symptoms onset stage was just a hypothetical one which was included in the model for simplicity. The individuals in *A* would then lose their transmissibility pathologically and transitioned into *R*. Meanwhile, individuals in *I* would either lose their transmissibility pathologically (*R*) before they got confirmed and isolated in hospital, which implies that a patient can be no longer infectious but still test positive or become isolated in hospital (*H*, lost their transmissibility physically) and eventually then lost their transmissibility pathologically (*R*). The parameters *r* and transmission rate (*b*) vary across five time periods based on key events (e.g., *Chunyun*, the period of intense travel preceding the Spring Festival) and containment interventions. Different from most of other dynamic models fitting number of confirmed diagnosis at time *t*, the numbers of individuals in all compartment in this model were not directly observable except in *I* where *I*(*t*) is the number of lab-confirmed cases who reported their date of symptoms onset was on time *t*.

In consideration of the SAPHIRE model described as above, the following four aspects can be potentially improved:

1) The initial ascertainment rate *r* was estimated based on the assumption of perfect ascertainments in Singapore ignoring asymptomatic individuals which certainly gave an over-conservative estimate of *r* under the current model as mentioned in Hao et al. (2020). In addition, *r* should be a continuous function rather than a step function over the five time periods, see the justification in Appendix D.

2) The individuals in *A* could be very different including asymptomatic, mild cases, and severe cases as evidence by deaths of clinically confirmed cases reported in (*2*), it is hence not optimal to assign a same transmission rate to all individuals in *A* (note that the proposed transmission rate in *A* was identical to that of the presymptomatic infectious period *P* and was α = 55% of that in *I*). At the beginning of the pandemic, the medical resources were overburdened. It was likely to have a larger fraction of patients with severe symptoms in *A* and thus the transmission rate would be close to that of *I*. When medical resources were replenished and strong screening and public awareness campaign were implemented, the remaining unascertained cases should mostly be asymptomatic or mildly symptomatic, and the transmission rate would be closer to that of *P*. See why this issue can not be easily resolved in Appendix D.

3) Though only the data of lab-confirmed cases were used in the SAPHIRE model, the isolation due to clinical diagnosis cannot be simply ignored in the model. As mentioned in Hao et al. (2020) the clinically diagnosed cases were excluded in the model. However, there were a significant number of cases in *A* of the SAPHIRE model who were not lab-confirmed but clinically confirmed and isolated in *fangcang* (square-cabin) hospitals in Wuhan during February 2020 and thus lost their transmissibility before they actually got into *R*, which implies that clinically-confirmed cases in *A* would have a faster rate to get into *R* than other cases in *A* (*3*).

4) The pre-determined symptomatic infectious period of D_i = 2.9 Days is questionable. The symptomatic infectious period D_i was the mean time from symptom onset to loss of transmissibility pathologically, and the value was calculated based on the claim that 44% of secondary cases were infected during the index cases' pre-symptomatic stage by He et al. (2020) (*4*). Regardless of whether such claim is correct (a matter arising paper to He et al. (2020) was published), this 44% of pre-symptomatic spread was estimated based on the confirmed cases with isolation measures outside Wuhan, which is certainly not appropriate to be used to estimate mean time from

symptom onset to loss of transmissibility pathologically. Furthermore, another defect in the calculation of D_i is the inconsistency in the study of Hao et al. (2020), where a constant infectiousness was assumed across the presymptomatic and symptomatic phases of ascertained cases in estimating D_i while in the meantime $\alpha = 0.55$ was used as the ratio of transmission rate of cases in P (presymptomatic) to that of in I (symptomatic). It is important to note that unlike other pre-determined parameters in the model, the value of D_i is quite crucial to the model estimates of interest, see Supplementary Table S1 in Appendix D for detail. Hence a more accurate choice of D_i is essential. It is worth to note that the clearance of all active infections in Hao et al. (2020) was predicted to occur on April 21 (April 8 to May 12), which was not consistent with the active cases detected in Wuhan in mid-May.

Appendix B: The modified SAPHIRE model

Inspired the SAPHIRE model in Hao et al. (2020), an improved dynamic model was proposed. The proposed model included 6 compartments: susceptible (S), exposed (E), presymptomatic infectious (P), infectious with significant symptoms (I), infectious without significant symptom (A), and removed (R). Note that patients in A could only transit to R by losing transmissibility pathologically while patients in I may reach R by either losing their transmissibility pathologically, isolating upon lab-confirmation, or isolating upon clinical diagnosis. Therefore, the transition rate from I to R is given by $D_i^{-1} + D_q^{-1} + D_c^{-1}$, where D_i and D_q are the period of the symptomatic infectious period and duration from illness onset to lab-confirmation; and D_c is the duration from illness onset to clinical diagnosis which varies at different time period (here let D_c equals to infinity and 10 days before and after February 2 in Wuhan).

Furthermore, it has been found that the transmissibility decays towards the end of infectious period, hence the assumption of a constant transmission rate b throughout compartment I and A might potentially lead to an overestimate of the effective reproduction number R_e in the early stages. A preliminary solution to this problem is to split I into IE (early stage of symptomatic infectious period with a higher transmissibility) and IL (late stage of symptomatic infectious period with a low transmissibility) and split A into AE (early stage of asymptomatic/mild infectious period with a higher transmissibility) and AL (late stage of asymptomatic/mild infectious period with a low transmissibility). The transition dynamics of these states are as follows:

(1) Let $IE \rightarrow IL$ and $AE \rightarrow AL$ with a rate of $1/D_i^e = 1/3$ which corresponds to the setting in the SAPHIRE model, while $IL \rightarrow R$ and $AL \rightarrow R$ with a rate of $1/D_i^l = 1/7$. Thus, the expectation of the symptomatic infectious period would be $3 + 7 = 10$ days which is consistent with the choice of $D_i = 10$ days.

(2) Individuals in IE have a transmission rate of b and individuals in AE have a transmission rate of αb.

(3) Individuals in IL have a transmission rate of $\beta_i b$ and individuals in AL have a transmission rate of $\alpha \beta_i b$, where $\beta_i, \beta_a \in [0,1]$ are the reduction factors of transmissibility in late stage and are unknown parameters to be inferred in the model.

Such modifications would grant us even better compartment homogeneity. See Supplementary Figure S1 for model illustration.

The ODE system of the above model is as follow:
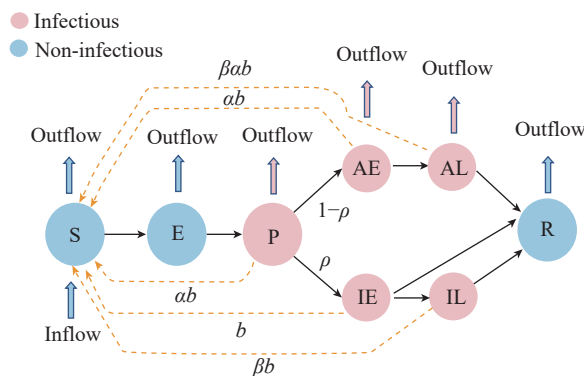
SUPPLEMENTARY FIGURE S1. Transmission dynamics of COVID-19 in Wuhan for modified SAPHIRE model .

$$\frac{dS}{dt} = n - \frac{bS\left(\alpha P + \alpha A_e + \alpha\beta_a A_l + I_e + \beta_i I_l\right)}{N} - \frac{nS}{N}$$

$$\frac{dE}{dt} = \frac{bS\left(\alpha P + \alpha A_e + \alpha\beta_a A_l + I_e + \beta_i I_l\right)}{N} - \frac{E}{D_e} - \frac{nE}{N}$$

$$\frac{dP}{dt} = \frac{E}{D_e} - \frac{P}{D_p} - \frac{nP}{N}$$

$$\frac{dA_e}{dt} = \frac{(1-\rho)\,P}{D_p} - \frac{A_e}{D_i^e} - \frac{nA_e}{N}$$

$$\frac{dA_l}{dt} = \frac{A_e}{D_i^e} - \frac{A_l}{D_i^l} - \frac{nA_l}{N}$$

$$\frac{dI_e}{dt} = \frac{\rho P}{D_p} - \frac{I_e}{D_i^e} - \frac{I_e}{D_q} - \frac{I_e}{D_c}$$

$$\frac{dI_l}{dt} = \frac{I_e}{D_i^e} - \frac{I_l}{D_i^l} - \frac{I_l}{D_q} - \frac{I_l}{D_c}$$

where b is the unknown transmission rate for significantly symptomatic cases in early stages and varies different time periods (set the five time periods as in Hao et al. (2020) for the demonstration in Wuhan); α is the ratio of the transmission rate of presymptomatic/asymptomatic/mild cases to that of significantly symptomatic cases and is prefixed; ρ is the unknown fraction of infections with significant symptoms; β_i and β_a are defined as before, set $\beta_i = \beta_a$ by assuming the trends of viral load are independent to symptoms; D_e, D_p, D_q, and D_c are the latent period, presymptomatic infectious period, duration from illness onset to isolation and duration from illness onset to clinical diagnosis respectively and are all predetermined. Under such setting, the transmission rate for AE is reasonable to be a constant over time and equal to the one for P. In addition, the lab-confirmation rate can be better presented as the function of the ratio between cases with insignificant (no/mild) and significant symptoms, and the time dependent ratio between the isolation/diagnosis and removal speed. Appendix E and F are for estimation method, choices of initial values, parameter settings, and sensitive analysis for the modified model.

Appendix C: Detailed results

The similar estimation method in Hao et al. (2020) is used in this study. Note that all CIs without further specifications are 95% CIs throughout this paper. The estimated cumulative number of infections up until March 8 was 194,302 (170,190–220,691) by fitting data from all 5 periods, this number increased to 198,748 (173,856–226,051) if the trend of the fourth period was assumed, 355,907 (301,525–418,579) if the trend of the third period was assumed or 11,507,840 (10,688,446–12,336,104) if the trend of the second period was assumed, see Supplementary Figure S2A–C for details. These represented a 2.24%, 44.16%, and 96.91% reduction of infections by the measures taken in the fifth period, the fourth and the fifth periods combined, and the last three periods combined, respectively. Note that under the trend of second period the total number of infections exceeded the total population of Wuhan. It was because the population inflow and outflow in Wuhan was about 800,000 per day before lockdown, the estimated number of infections could therefore be regarded as the number of infection in/from Wuhan.

The number of daily active infections (including cases in P, I, and A) peaked at 75,093 (64,342–87,068) on February 1 and dropped to 6 (1–13) on May 14 (Supplementary Figure S2D). If the trend remained unchanged as in the fifth period, the number of significantly symptomatic infections (I) would first become zero on April 12 (April 3 to April 23), and the clearance of all infections (namely $E + P + I + A = 0$) would occur on June 4 (June 15 to July 5). Compared with the estimates in Hao et al. (2020), the estimate on A was much more heavily tailed implying the high covertness of COVID-19. Considering a few cases detected in Wuhan in mid-May, the estimate on the clearance of all active infections was more consistent with the official report in Wuhan than what was predicted in Hao et al. (2020) (5–6).

Regarding continuous surveillance and interventions, based on the modified model that if control measures were lifted after zero new reported case in a consecutive period of 14 days, the probability of resurgence, defined as the number of active significantly symptomatic cases greater than 100, was still as high as 0.72, and the surge was
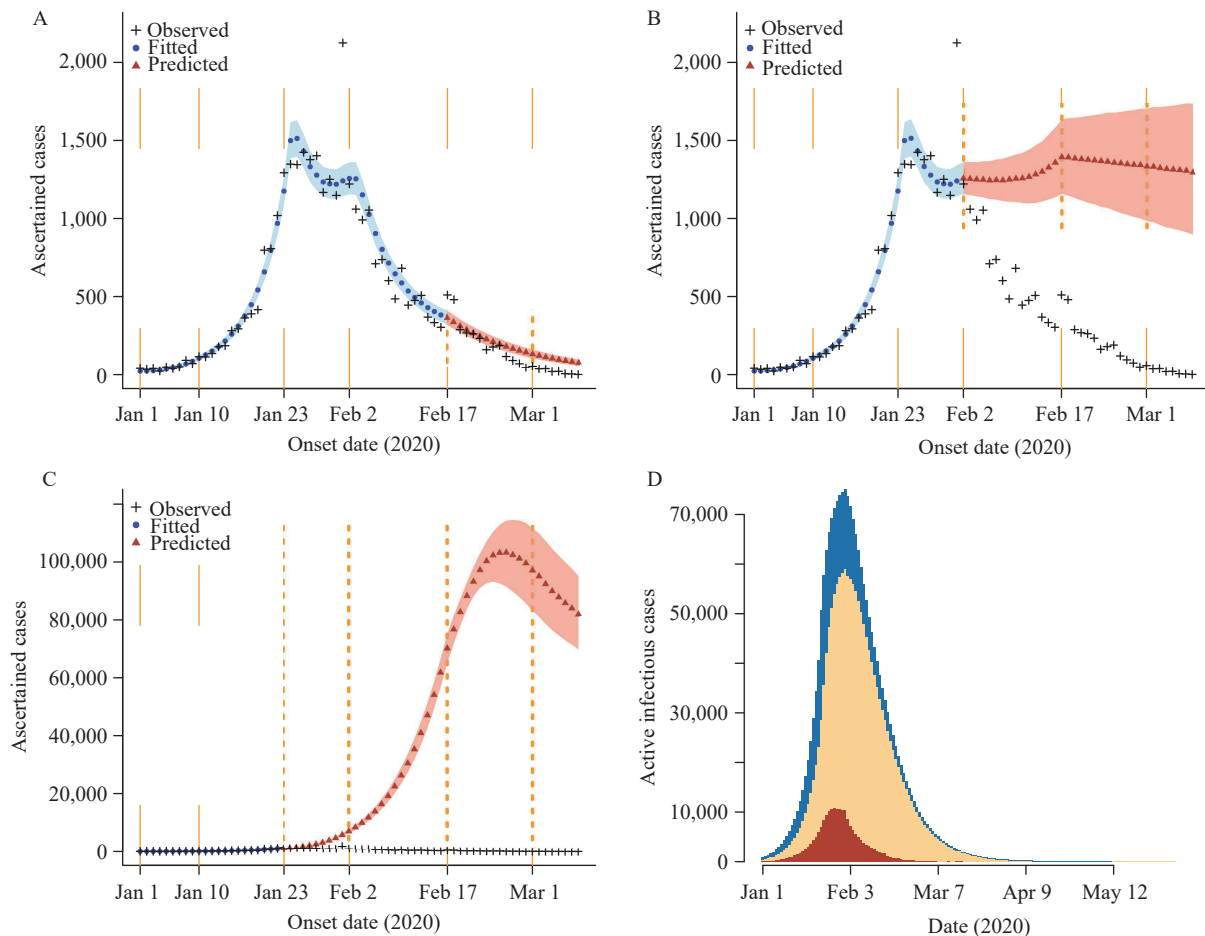
SUPPLEMENTARY FIGURE S2. Results of secondary analysis: epidemic trends under hypothetic policies, and estimations of standing active virus carriers. (A) Prediction using parameters estimated from the fourth period (February 2–16). (B) Prediction using parameters estimated from the third period (January 23 to February 1). (C) Prediction using parameters estimated from the second period (January 10 to January 22). The shaded areas are 95% credible intervals, and the colored points are the mean values based on 20,000 MCMC samples. (D) Estimated number of pre-symptomatic infections (P, in blue), infections without significant symptoms (A, in yellow) and infections with significant symptoms (I, in red) in Wuhan.

predicted to occur on Day 41 (31–57) after lifting controls. Compared with the results in Hao et al. (2020), estimates on the probability of resurgence were much higher, which suggests continuous efforts in interventions is essential to contain the spread of the pandemic.

Appendix D: Detailed explanation to issues in Hao et al. (2020)

The mean transmissibility in A defined by Hao et al. (2020) should be a time/configuration dependent function $\alpha(t)$, which were determined by averaging the transmissibility between patient with symptoms and those with no/mild symptom in A. Unfortunately, these two sub-populations of A were unidentifiable in the proposed model structure by Hao et al. (2020). One relatively easy potential fix of the issue was to replace αA with $\alpha_i A$ and allow α_i changing over different time steps in the paper. However, according to the definition of A, patients that did not get diagnosed could only increase through symptom onset and decrease through the loss of infectivity. Thus, the evolution of the sub-population proportion within A must be continuous in time. Meanwhile, the changes in containment measures/lab-confirmed rates in different steps in this model could only lead to changes to the evolution rate but not the proportion itself. This fact made it inappropriate to treat α as a step function. By similar argument, the setting of r in Hao et al. (2020) as a step function is also questionable.

SUPPLEMENTARY TABLE S1. Sensitivity analysis on the choice of D_i the SAPHIRE model. With a longer infectious period, it is expected to obtain a higher reproduction number in the beginning of the epidemic and a longer time needed to clear all infections in the Wuhan.

D_i (days)	Ascertainment rate	R_e in Period 1	R_e in Period 2	R_e in Period 3	R_e in Period 4	R_e in Period 5	Date of the clearance of all infections
2.9	12.7% (10.2%−15.6%)	3.54 (3.41−3.68)	3.32 (3.20−3.45)	1.18 (1.11−1.25)	0.51 (0.47−0.54)	0.28 (0.23−0.32)	April 21 (April 8 to May 12)
5	12.2% (9.8%−15.1%)	4.16 (4.00−4.33)	3.80 (3.65−3.95)	1.37 (1.28−1.45)	0.49 (0.45−0.52)	0.21 (0.18−0.26)	May 7 (April 21 to May 30)
7	12.1% (9.8%−15.1%)	4.68 (4.48−4.88)	4.18 (4.00−4.35)	1.56 (1.45−1.67)	0.49 (0.45−0.53)	0.18 (0.15−0.22)	May 28 (May 9 to June 25)
9	11.9% (9.5%−14.7%)	5.12 (4.89−5.35)	4.48 (4.28−4.68)	1.76 (1.65−1.89)	0.51 (0.47−0.55)	0.16 (0.13−0.20)	June 21 (May 31 to July 19)
13	11.1% (8.9%−13.7%)	5.83 (5.56−6.10)	4.93 (4.71−5.14)	2.18 (2.03−2.34)	0.57 (0.52−0.61)	0.15 (0.12−0.19)	July 19 (July 18 to July 19)

Appendix E: Estimation method

A major obstacle in parameter inference of the modified model is that now no compartment is directly observable. To be precise, $I(d)$ is the inflow of I on day d satisfying a Poisson distribution with $\lambda_d = \rho P_{d-1} D_p^{-1}$, while the observed data only consisted of those who had symptoms onset on day d provided that they would be diagnosed in the future, namely, a sub-population in I. Therefore, the distribution of such sub-population was estimated under this model. Fortunately, by the thinning argument of a Poisson process, the size of the sub-population of interest satisfies Poisson distribution with $\bar{\lambda}_d = rP_{d-1}D_p^{-1}q_d$, where q_d is the probability that a patient with symptom onset on day d would be diagnosed in the future. Moreover given D_n, the duration from symptom onset to the time point that test turns to negative, and D_q are predetermined in Hao el al (2020), the exact value of q_d can be independently calculated using the following stochastic viewpoint of the dynamic model: consider $N_1(t)$ a time-dependent Poisson Process/Poisson Point Measure, with intensity equals to $D_q(d) = 21, 15, 10, 6, 3$ on different stages, and $N_2(t)$ a time homogeneous Poisson Process with intensity D_n independent to N_1. For each d, define stopping times

$$\tau_{d,1} = \inf\{t \geq d, N_1(t) = N_1(t-) + 1\}$$

and

$$\tau_{d,2} = \inf\{t \geq d, N_2(t) = N_1(t-) + 1\}$$

be the first jumps times after d. Then q_d can be calculated can the probability that $\tau_{d,1} < \tau_{d,2}$. The specific values of q_d can either be calculated manually for each d or can be approximated numerically using frequencies obtained from multiple independent stochastic simulations. Since the precision of numerical simulation can be guaranteed by law of large numbers and large deviation theory, it was used here to approximate the values of q_d's with 10^5 stochastic realizations for each d.

Appendix F: Choices of initial values, parameter settings and sensitive analysis

Supplementary Table S2 provides a list of parameter settings in the modified model for all five periods. The initial values of I, A were estimated as follows:

(1) Let $I^c(0)$ the number of symptoms onset cases during December 29 to 31 who would be lab-confirmed in the future; $r_0 = 0.23$ be the initial lab-confirmed rate in Wuhan among symptomatic case which was calculated based on assuming complete diagnosis of early cases among symptomatic cases in Singapore; and $\rho_0 = 0.7$ be the proportion of symptomatic patients (1,7–9).

(2) The initial population of symptoms onset patients in Wuhan namely $A(0) + I(0)$ were hence given by $I^c(0) r_0^{-1} \rho_0^{-1}$.

(3) The ratio between $A(0)$ and $I(0)$, it should be roughly the same as the unknown diagnosable ratio ρ in the ODE system of the modified model. By "fix point iteration" method, ρ was estimated to be 0.26, hence $I(0) = 0.26 I^c(0) r_0^{-1} \rho_0^{-1}$ and $A(0) = 0.74 I^c(0) r_0^{-1} \rho_0^{-1}$.

(4) $AE(0) = A(0) D_i^e/D_i, AL(0) = A(0) D_i^l/D_i, IE(0) = I(0) D_i^e/D_i, IL(0) = I(0) D_i^l/D_i$.

In the original paper, $P_I(0)$ and $E_I(0)$ stood for the numbers of lab-confirmed cases with onset during January 12,

SUPPLEMENTARY TABLE S2. Parameter settings for five periods.

Parameter	Meaning	Jan 1−9	Jan 10−22	Jan 23−Feb 1	Feb 2−16	Feb 17−Mar 8
b	Transmission rate of significant cases	b_{12}	b_{12}	b_3	b_4	b_5
ρ	Fraction of infections with significant symptoms or diagnosable ratio	ρ	ρ	ρ	ρ	ρ
α	Ratio of transmission rate of no/mild symptomatic patients to that of significantly symptomatic patients	0.55	0.55	0.55	0.55	0.55
D_e	Latent period	2.9	2.9	2.9	2.9	2.9
D_p	Presymptomatic infectious period	2.3	2.3	2.3	2.3	2.3
D_q	Duration from illness onset to lab-confirmation/isolation	21	15	10	6	3
D_n	Duration from symptom onset to negative test result	14	14	14	14	14
D_c	Duration from symptom onset to clinical-confirmed diagnosis/isolation	∞	∞	∞	10	10
N	Population size	10,000,000	10,000,000	10,000,000	10,000,000	10,000,000
n	Daily inbound and outbound size	500,000	800,000	0	0	0

2020 and during January 3 to 5, 2020. According to the same reasonings as for $A(0) + I(0)$, there were $E(0) = E_I(0)\, r_0^{-1}\rho_0^{-1}$ and $P(0) = P_I(0)\, r_0^{-1}\rho_0^{-1}$. The estimates of parameters of interest were given in Supplementary Table S3 with a sensitivity analysis on D_n. Note that it was reasonable to believe that the mean duration from symptom onset to negative test result is less than 21 days, $D_n = 14$ was used in the main model (see upper left panel of Supplementary Figure S2 in (4) for reference). The estimates are relatively robust to the different choice of D_n.

SUPPLEMENTARY TABLE S3. Estimated transmission rates, overall lab-confirmation rate, and diagnosable ratio from the sensitivity analysis where $D_n = 14$ is used in the main model.

	r	b_{12}	b_3	b_4	b_5	ρ	$\beta i=\beta a$
D_n=10	0.18(0.16, 0.21)	1.01(0.91,1.10)	0.20(0.18, 0.23)	0.10(0.08, 0.13)	0.07(0.05,0.1)	0.32(0.28, 0.37)	0.40(0.17, 0.66)
D_n=14	0.17(0.15, 0.19)	1.03(0.94, 1.13)	0.21(0.18, 0.24)	0.10(0.08, 0.12)	0.07(0.05,0.09)	0.26(0.23, 0.29)	0.46 (0.22, 0.71)
D_n=21	0.15(0.13, 0.17)	1.06(0.97,1.15)	0.22(0.19, 0.24)	0.10(0.08, 0.12)	0.06(0.04,0.09)	0.20(0.18, 0.23)	0.48(0.24, 0.73)

REFERENCES

1. Hao XJ, Cheng SS, Wu DG, Wu TC, Lin XH, Wang CL. Reconstruction of the full transmission dynamics of COVID-19 in Wuhan. Nature 2020;584:420 – 4. http://dx.doi.org/10.1038/s41586-020-2554-8.
2. Health Commission of Hubei Province. Situation report on 12 February 2020. http://wjw.hubei.gov.cn/bmdt/tzgg/202002/t20200213_2025582.shtml. [2021-01-15]. (In Chinese).
3. 10, 000 new "clinical diagnosed cases" confirmed in a day in Hubei. 2020. https://news.sina.cn/gn/2020-02-13/detail-iimxyqvz2457971.d.html. [2021-01-15]. (In Chinese).
4. He X, Lau EHY, Wu P, Deng XL, Wang J, Hao XX, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. Nat Med 2020;26:672 – 5. http://dx.doi.org/10.1038/s41591-020-0869-5.
5. Wuhan ended its 35 days of zero new cases. 2020. https://news.ifeng.com/c/7wNzkK9Br6a.[2021-01-15]. (In Chinese).
6. City-wide screening results (5 days) released in Wuhan, 58 new asymptomatic cases detected. 2020. http://www.sanyarb.com.cn/content/2020-05/20/content_495360.htm. [2021-01-15].
7. Hu ZL, Song C, Xu CJ, Jin GF, Chen YL, Xu X, et al. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. Sci Chin Life Sci 2020;63:706 – 11. http://dx.doi.org/10.1007/s11427-020-1661-4.
8. Nishiura H, Kobayashi T, Suzuki A, Suzuki A, Jung S, Hayashi K, et al. Estimation of the asymptomatic ratio of novel coronavirus infections (COVID-19). Int J Infect Dis 2020. http://dx.doi.org/10.1016/j.ijid.2020.03.020.
9. Zhang Y, You C, Cai ZH, Sun JR, Hu WJ, Zhou XH. Prediction of the COVID-19 outbreak in China based on a new stochastic dynamic model. Sci Rep 2020. http://dx.doi.org/10.1038/s41598-020-76630-0.

Notes from the Field

COVID-19 Case Likely Caused by Contaminated Object During Hotel Disinfection — Guangxi Zhuang Autonomous Region, China, January 2021

Jiatong Zhuo[1,#]

On January 13, 2021 in Nanning City of Guangxi Zhuang Autonomous Region, an individual (Patient A) tested positive for coronavirus disease 2019 (COVID-19). Patient A provided a disinfection service for a business hotel in Nanning that was designated by the government to accept international travelers entering China and quarantine the travelers for 14 days. Patient A had no history of travel and had previously tested negative for COVID-19 twice on January 4 and January 11, 2021.

From December 29, 2020 to January 13, 2021, Patient A mostly traveled by electronic scooter and wore personal protective equipment (PPE) diligently. Since there have been no domestic cases reported in Nanning recently, he was not likely to be infected through person-to-person aerosol transmission. He performed his disinfection work 9 times during the roughly 15-day period in the business hotel and was likely infected through a person-to-material route by a traveler returning from Indonesia. The traveler had stayed at the business hotel for a 14-day period, had tested negative twice, and was released on January 13 to return home to Shanxi. However, on January 20, the traveler tested positive for COVID-19 nucleic acids as well as IgM and IgG antibodies; he was subsequently diagnosed as an asymptomatic carrier of COVID-19.

Based on this finding, we believed Patient A's PPE was contaminated with COVID-19 during his management of the disinfection service. In addition, Nanning also had abnormally cold weather during this period as the city remained under 10 °C from December 29, 2020 to January 13, 2021, which likely helped keep the virus active. This evidence suggests that Patient A's PPE were likely contaminated during his disinfection activities in the hotel, and he likely became infected after using his hands to touch his PPE and then touching his mouth, nose, or eyes.

This material-to-person route of transmission has been reported in previous incidents including outbreaks stemming from a dockworker in Qingdao (*1*), a cargo worker at Shanghai's Pudong Airport (*2*), and the Xinfadi Wholesale Market in Beijing (*3*). This suggests that current disinfection protocols (*4*) should be improved so that workers are more vigilant while removing their PPE and will adhere more closely to post-disinfection protocols, including washing hands and not touching contaminated surfaces and objects.

REFERENCES

1. Yuan Q, Kou ZQ, Jiang FC, Li ZJ, Zhang LJ, Liu HH, et al. A nosocomial COVID-19 outbreak initiated by an infected dockworker at Qingdao City Port — Shandong Province, China, October, 2020. China CDC Wkly 2020;2(43):838 – 40. http://dx.doi.org/10.46234/ccdcw 2020.224.
2. Fang FH, Song Y, Hao LP, Nie K, Sun XD. A case of COVID-19 detected in a cargo worker at Pudong airport — Shanghai Municipality, China, November 8, 2020. China CDC Wkly 2020;2(47):910 – 1. http://dx.doi.org/10.46234/ccdcw2020.246.
3. Tan WJ, Niu PH, Zhao X, Pan Y, Zhang Y, Chen LJ, et al. Reemergent cases of COVID-19 — Xinfadi wholesales market, Beijing Municipality, China, June 11, 2020. China CDC Wkly 2020;2(27):502 – 4. http://dx.doi.org/10.46234/ccdcw2020.132.
4. Wang JQ, Zhang BY, Duan HY, Liang C, Sun HH, Zhang J, et al. Key points of the program for disinfection technology in special places during the Coronavirus Disease-2019 (COVID-19) outbreak. China CDC Wkly 2020;2(9):140 – 2. http://dx.doi.org/10.46234/ccdcw2020.038.

Four COVID-19 Cases of New Variant B.1.351 First Emerging in South Africa in Chinese Passengers on Same Flight — Shenzhen, China, January 2021

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At 04:50 on January 1, 2021, a 36-year-old Chinese project manager (Case A), a 29-year-old Chinese worker (Case B), and a 53-year-old Chinese businessman (Case C) returned from Africa (Case A and B from South Africa and Case C from Lesotho) on the same flight and tested coronavirus disease 2019 (COVID-19) RNA positive by real-time polymerase chain reaction (PCR) by Baoan District People's Hospital. Shenzhen CDC received their oral nasopharyngeal swabs packages from the hospital and retested COVID-19 RNA positive at 09:50. Meanwhile, Case D, a close contact of Case A, was transferred to the designated hotel for centralized isolation for 14 days. His oral nasopharyngeal swabs were collected and sent for the detection of COVID-19 RNA as routine surveillance testing on the 1, 4, 7, 14 days of quarantine; these were reported back as COVID-19 RNA positive at 22:50 on January 4, 2021 and at 05:30 on January 5, 2021 by Shenzhen CDC. The four cases were transferred respectively by negative pressure ambulances to the Third People's Hospital of Shenzhen for further treatment within five hours of COVID-19 infection confirmation by Shenzhen CDC. On admission, chest CT images showed no abnormalities among all cases.

Epidemiological investigation revealed that the 4 cases had COVID-19 RNA negative test results before departure and self-reportedly had effective protection by wearing medical protective masks (Case A wore a disposable medical mask, while Case B, C, and D wore N95 masks) and protective suits (Case B) during the flight. In addition, they reported no history of fever, fatigue, or respiratory symptoms within 14 days prior to their diagnosis. However, according to the report of Case A, he was possibly exposed on his return business trip from Cape Town to Johannesburg in South Africa from December 16 to December 30, 2020, when he visited and had dinner with colleagues and had a meal in a fast food restaurant. Case B had a history of performing work-related tasks, staying at the dormitory with workmates. His roommate, who took the same flight from South Africa to China, was diagnosed as an asymptomatic carrier of COVID-19 on January 1, 2021 in Shenzhen. Case C's potential exposure might have been a 4-hour-trip in a vehicle from his company in Lesotho to an airport hotel with a local resident without effective protection. Case D's potential exposure was the experience that he took nucleic acid testing in South Africa and shuttle bus from workplace to the airport with Case A before boarding. Using the results of the epidemiological investigation, clinical symptoms, and laboratory results, these patients were diagnosed as asymptomatic patients with COVID-19 in coordination with clinicians and experts.

The specimens of the 4 asymptomatic patients' were sequenced by Illumina MiSeq Sequencing platform between January 2 to January 5, 2021. On January 4 and January 7, 3 whole genome sequences and 1 were obtained, respectively. Compared with the Wuhan reference sequence (EPI_ISL_402119) (1–2), these 4 newly identified Shenzhen strains showed 29 nucleotide variation sites, which contained the single nucleotide polymorphisms (SNPs) that defined lineage B.1.351 (20H/501Y.V2 branch) (3). A maximum of 29 genomic variation sites were detected in the 4 high-quality genomic sequences (for Cases A–D, number of genomic variation sites were 29, 19, 25, and 25, respectively, including G160A, G174T, C241T, C281T, C1059T, C3037T, G5230T, C8660T, C8964T, A10323G, G11230T, T13324A, C14408T, C14925T, T16062C, G19656T, A21801C, G22299T, G22813T, G23012A, A23063T, A23403G, C23664T, T25084C, G25563T, C25904T, C26456T, C28647T, C28887T; sequence coverage ranged from 91.4% to 99.2%). A major difference between the nucleotide sequences of A/D

and B/C were detected in the position of 1174 (A1174C for A/D and A1174T for B/C). By online comparison of the assembled sequence with the published COVID-19 database, we obtained the phylogenetic relationship tree (Figure 1) of the virus strains. The 4 COVID-19 samples of imported African cases were lineage B.1.351 (20H/501Y.V2) variant strains (homology of 99.99% to 100%), which had been circulating in South Africa since October 2020 (*4*). The cladogram showed that the genome sequences of the 4 cases imported from Africa (Case A–D) all contained the characteristic mutation sites (the mutations of the spike protein D80A, K417N, E484K, N501Y, D614G, and A701V) of the South African variant strain B.1.351. The major differences between the A/D and B/C when comparing their amino acid sequences were as follows: L18F was detected in Case C; D215G was detected in Case B/C; R246I was detected in Case A; but data on the same position was missing in Case D. These B.1.351 variants strains were imported early to China and might exert a great threat to the prevention and control of COVID-19 in China. Systematically tracking higher risk international variants is therefore important as it allows monitoring of the new variants nationally and internationally.

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REFERENCES

1. Tan WJ, Zhao X, Ma XJ, Wang WL, Niu PH, Xu WB, et al. A novel coronavirus genome identified in a cluster of pneumonia cases — Wuhan, China 2019–2020. China CDC Wkly 2020;2(4):61 – 2. http://dx.doi.org/10.46234/ccdcw2020.017.
2. Zhu N, Zhang DY, Wang WL, Li XW, Yang B, Song JD, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382(8):727 – 33. http://dx.doi.org/10.1056/NEJMoa2001017.
3. Rambaut A, Holmes EC, O'Toole á, Hill V, McCrone JT, Ruis C, et al. A dynamic nomenclature proposal for SARS-CoV-2 lineages to assist genomic epidemiology. Nat Microbiol 2020;5(11):1403 – 7. http://dx.doi.org/10.1038/s41564-020-0770-5.
4. Tegally H, Wilkinson E, Giovanetti M, Iranzadeh A, Fonseca V, Giandhari J, et al. Emergence and rapid spread of a new severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) lineage with multiple spike mutations in South Africa. medRxiv. 2020. http://dx.doi.org/10.1101/2020.12.21.20248640v1.

FIGURE 1. Phylogenetic tree based on the complete genome sequences of severe acute respiratory syndrome coronavirus 2 virus.

The four imported 501Y.V2 cases are colored in red letters. Scale bar indicates nucleotide substitutions per site. The lineages and sublineages of COVID-19 virus are marked and colored on the right.

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