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Original Article

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Characteristics of post-Wuhan COVID-19 outbreaks in mainland China

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Abstract

Objective: To review the characteristic of Coronavirus disease 2019 (COVID-19) outbreaks in mainland China, particularly post-Wuhan outbreaks, and to help design effective responses in the foreseeable future.

Method: The data regarding COVID-19 outbreaks between December 2019 and March 16, 2022 were obtained from China's publicly available databases. The data were analyzed using descriptive statistics. Five outbreak stages were defined according to distinct epidemiological characteristics across different time periods over the past two years.

Result: Since the 2020 Wuhan outbreak, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) local infections were confirmed in 37 995 cases as of March 16, 2022. We identified 285 isolated outbreaks in unrelated people that occurred in four additional distinct stages, over 57% of which had been imported, such as imported infected travelers and fomite transmission. The basic reproduction number (R0) of original SARS-CoV-2 was about 2.79, while the Delta variant was about 5.08 and Omicron was 7.0 or greater, resulting in the disease being more contagious during the fourth (Delta) and fifth (Omicron) stages than previous stages.

Conclusion: China has experienced various COVID-19 outbreaks of different levels since the start of the pandemic in Wuhan, and local transmission is mainly caused by imported sources. If the "dynamic COVID-zero" policy is not appropriately followed, it will be difficult to contain the spread in China from overseas and to cope with the Omicron variant.

KEYWORDS: COVID-19; Post-Wuhan; Four outbreak stages; Characteristics

1. Introduction

For more than two years, the coronavirus disease 2019 (COVID-19) pandemic has engulfed the world, causing devastating impacts on the global public health system. Since severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is highly transmissible, infections have been confirmed in more than 461 million people and more than 6 million have died as of March 16, 2022[1]. In December 2019, the first COVID-19 cluster of China was reported in the area around the Huanan Seafood Supermarket in Wuhan, the capital of Hubei Province. A month later, the central government of China imposed a strict lockdown on the entire region to quarantine the center of the outbreak. On April 8, 2020, the Wuhan lockdown was officially ended, which marked the end of the first domestic stage

Significance

Few studies are available on the overall evolution of COVID-19 outbreaks. Our study provided a general description of post-Wuhan outbreaks in China, suggesting that controlling domestic transmission caused by imported cases is still a huge challenge, which helps in learning more about SARS-CoV-2 transmission and implementing prevention and control measures for COVID-19.

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of the pandemic(December 2019 to April 7, 2020) in mainland China (Supplementary Figure S1). Since the reopening of Wuhan, however, viral transmission has continued: another 41650 confirmed cases of COVID-19 (15573 imported and 26077 domestic) have been officially reported as of March 16, 2022(Supplementary Table S6). With the emergence of new variants and the reemergence of infections, the current situation continues to develop, and the consequences remain uncertain.

In the early stages of the pandemic, because effective drugs and vaccines were unavailable, local governments worldwide adopted many common measures, including travel limitations, school and workplace closures, and cancellation of public events to halt the spread of COVID-19[2]. Countries throughout the world had different perspectives about the disease and used different strategies accordingly to cope with. These strategies can be generally categorized into three types: aggressive containment, suppression, and mitigation[3]. China's responses have been characterized by three phases of prevention and control: the emergency containment, the exploratory normalization, and the "dynamic COVID-zero" phase across the whole chain[4]. The containment and "dynamic COVID-zero" policies have been more aggressive and more effective than those employed in the rest of the world: the reported cases constitute fewer than 0.05% of the total global number of cases given the population is more than 19% of the world's population[5].

Some research on COVID-19-related progression has focused on specific places, whereas other studies concentrated on particular incidents: these approaches have limited the assessment of virus transmission and of prevention and control strategies. Little is currently known about the overall evolution of COVID-19 outbreaks in China, especially post-Wuhan outbreaks. Thus, in this study, we collected and summarized information regarding all domestic infections that occurred after the Wuhan lockdown in mainland China (the first stage), grouped those infections into four additional stages, and described the characteristics of and responses to these four stages. This review provided a general depiction of the post-Wuhan outbreaks with which to accumulate more understanding of SARS-CoV-2 and to help in predicting future epidemics and designing effective public responses in the foreseeable future.

2. Methods

2.1. Data collection

We gathered information regarding COVID-19 outbreaks from December 2019 to March 16, 2022. The general data used in this study were obtained from the official website of the National Health Commission of the People's Republic of China, which established a database of China's COVID-19 cases that provides official real-time updates and ensures the reliability of data. The detailed data were obtained from the health commissions of provinces and their prefecture-level cities and news outlets in mainland China. We attempted to track down all domestic cases of both symptomatic and asymptomatic infections in mainland China. By determining which cases were interconnected, we grouped a total of 37995 domestic cases into 285 incidents (Supplementary Tables S2-S5), each of which was an independent outbreak with the same transmission chain of infections among one or several provinces. A small number of incidents were reported together without an understanding of different transmission chains at the beginning of the study, which, however, could have been associated with at least one transmission chain.

2.2. Data analysis

In accordance with distinct epidemiological characteristics across different time periods over the past two years, we categorized all 285 post-Wuhan incidents into four indigenous stages in mainland China. According to our definitions, the first stage (Wuhan outbreaks) included all infections from the very first batch of cases to the end of the initial Wuhan lockdown; the second stage covered the period after the end of the Wuhan lockdown until a 56-day period in which zero domestic infections were confirmed which was followed by the third stage, in which the Delta variant first identified in India caused a deadly outbreak in India early in 2021. The Delta strain is estimated to be more than twice as transmissible as the original strain and quickly become the dominant strain globally in June 2021[6,7]. The fourth stage in China began with the first local identification of the Delta variant. The next significant variant was the Omicron strain, which multiplies in the human bronchus approximately 70 times faster than the Delta strain; however, evidence suggests that it causes less severe disease than did previous strains, especially Delta[8]. The fifth stage started when the ongoing Omicron variant was identified in China.

The collected information was summarized according to the infected populations, sites, duration (days between when the first and last cases were identified), genome sequence, potential sources of infection, news resources, and other relevant information regarding each incident. Detailed information is listed in the supplementary tables. Two independent researchers reviewed and analyzed the data. Because the data were retrieved from publicly available databases, no informed consent from patients was required. We used Adobe Illustrator, Version 2021 (Adobe, San Jose, CA, USA), to construct the figures.

3. Result

During the first domestic stage, the disease spread from Wuhan to 31 other provinces of mainland China, with a total of 80760 domestic cases and 1042 imported cases (Supplementary Table S1). Hubei Province alone reported an infection rate of 84% (Supplementary Figure S1). The first stage peaked on February 12, 2020, with 6000 positive cases. During this period, all domestic cases were linked with exposure to a case in Wuhan or Hubei Province.

During the second domestic stage (April 8 to September 23,

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2020), infection linked to cases in Wuhan and Hubei Province and a rising number of imported cases were reported. We identified 137 independent domestic incidents, with a total of 3 126 domestic cases (1 466 symptomatic and 1 660 asymptomatic). The frequency of incidents gradually declined toward the end of this stage from 93 times in April to 30 in May, 11 in June, two in July, and only one in August (Figure 1 and Figure 2A; Supplementary Table S2). After the lockdown ended in Wuhan, thousands of residents left the area for work and travel, which led to 78 linked incidents. Popular destinations of the travelers consequentially became the hotspots of outbreaks, for example, the municipality city of Chongqing had 28 incidents, and Guangdong Province had nine incidents. This aftermath phenomenon was brief, and the last Wuhan-linked case (an asymptomatic one) was identified in Chengdu, in Sichuan Province on June 21, 2020.

The third domestic stage (September 24, 2020, to May 20, 2021) was partly linked to imported sources. During this stage, 33 independent domestic incidents were reported with a total of 3 749 domestic cases (2 478 symptomatic and 1 271 asymptomatic). The majority of incidents occurred in northern China and during the last three coldest months: five in November, 11 in December, and six in January (Figure 1, Figure 2B and Supplementary Table S3). The incident in Dalian, Liaoning Province (1 742 cases identified in 56 d), which began with five workers at the Port of Dalian, led to infections in seven cities of five provinces. Later, the genomic information of the virus revealed that this strain was of Russian lineage. After that winter, the frequency of incidents fell again: in the four months after March, only seven incidents occurred. One asymptomatic case occurred in Xi'an, Shaanxi Province; one symptomatic case in Jiujiang, Jiangxi Province; 118 cases in 22 d in Ruili, Yunnan Province.

The fourth domestic stage (May 21 to December 2, 2021) began with the first reported domestic case of the Delta variant in Guangzhou, Guangdong Province. During this period, 25 independent domestic incidents were reported, with a total of 7 084 domestic cases (6 729 symptomatic and 354 asymptomatic). Of the incidents, 40% were associated with an infected person returning from overseas, 20% were associated with imported fomite transmission, and 4% were identified with overseas genomic lineage, although the detailed association was unknown. Cases of COVID-19 were reported in all provinces of mainland China except for Tibet. The Delta variant caused most of the incidents and spillovers during this period; the incident in Nanjing, Jiangsu Province (1 162 cases identified in 46 d) was the largest outbreak at that time, and the incident in Xi'an, Shaanxi Province (which involved infections in at least 36 cities of 16 provinces), represented the largest virus spillover (Figure 1 and Figure 2C; Supplementary Table S4). For example, the Nanjing Lukou International Airport coronavirus cluster, caused by the Delta strain and linked to a flight from Russia, spread to 11 other provinces, resulting in 1 162 reported cases. The other two provinces with the highest numbers of infections were Hubei (162 cases) and Hunan (129 cases). During this stage, the average number of infections per incident was 283 and most incidents were quickly contained during two maximum incubation periods (which lasted four weeks).

The fifth domestic stage (beginning December 3, 2021) started with the first domestic infection with the Omicron variant in Guangzhou, Guangdong Province, and is characterized by both Delta and Omicron variants. During this stage, 90 independent domestic incidents were reported as of March 16, 2022, with a total of 24 036 infections. Of these incidents, 21.1% were associated with an infected traveler returning from overseas, 14.4% were associated with imported fomite transmission, and 28.9% were identified with overseas lineage, although the detailed association was unknown. Additionally, source information was unavailable for 35.6% of the incidents because most of these have not yet ended, and the information may be undeclared. The Omicron variant, especially its subvariant BA.2, has fueled a rapid widespread surge and local outbreaks with complex transmission chains. More than 15 000 infections in 28 provinces were reported from March 1 to 16, 2022, and more than 2 000 new infections were detected in the mainland for three consecutive days, which far exceeded the regular scale of infection during the 2020 Wuhan outbreak (Figure 1 and Figure 2D; Supplementary Table S5). In the northeast, the highly transmissible Omicron variant caused 11 822 cases identified as of March 16, 2022 and spread to at least eight provinces, the majority affecting Jilin

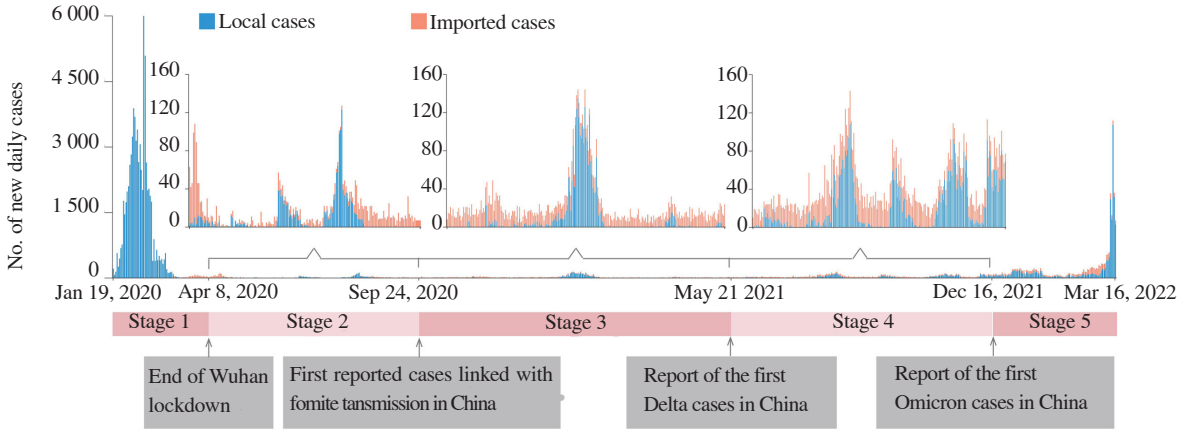

Figure 1. Daily report of confirmed cases of coronavirus disease 2019 (COVID-19) in mainland China with major relevant events in different stages as of March 16, 2022.

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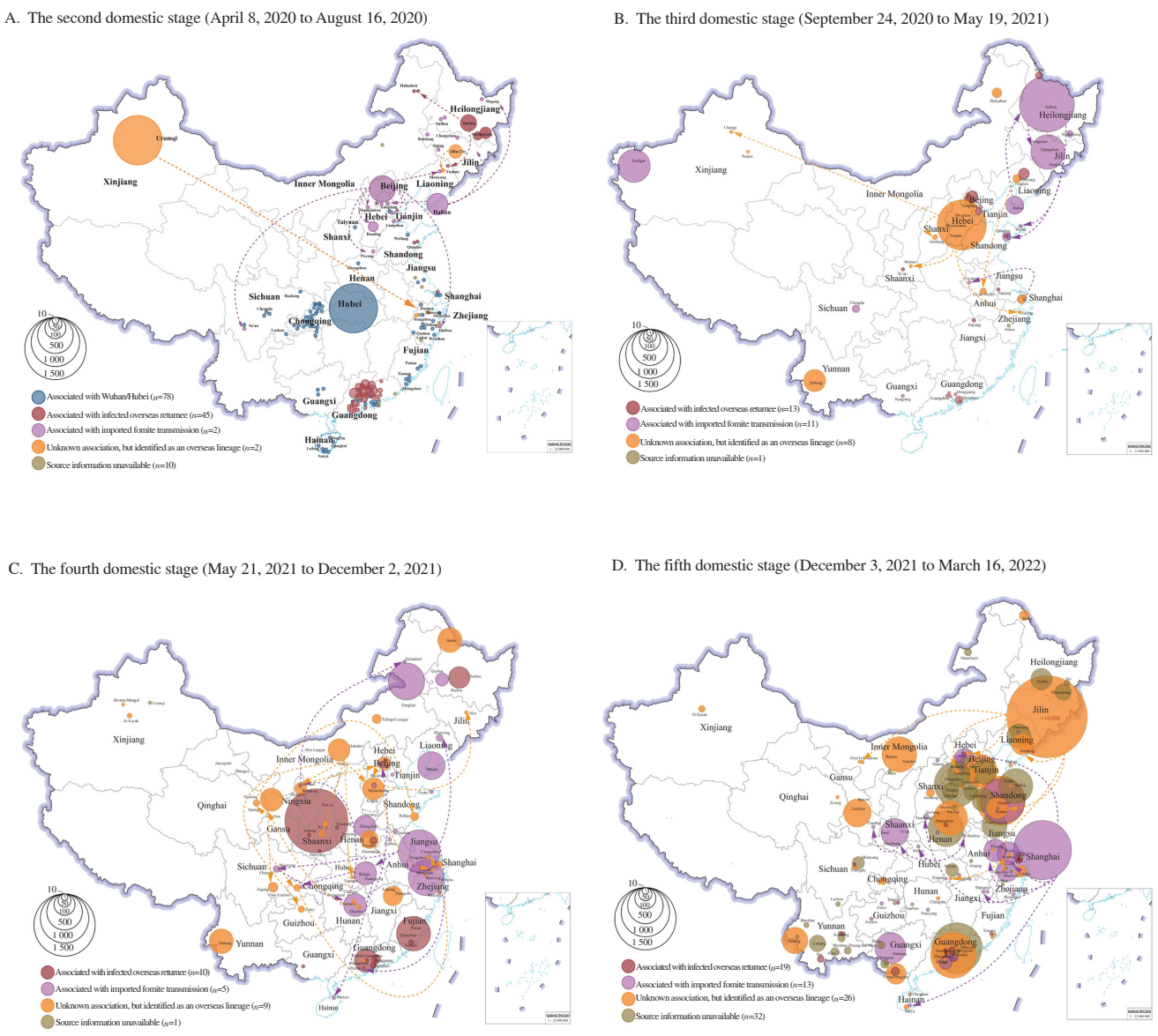

Figure 2. Distribution and potential sources of confirmed cases of coronavirus disease 2019 (COVID-19) in the second (A), third (B), fourth (C), and fifth (D) stages in mainland China. The circles represent the sizes of each incident, and the colors indicate potential sources. The cities named were those where an incident was identified. Arrows indicate the travel routes within individual incidents (which do not include the cases that originated in Hubei Province). The arrows for the fourth and fifth stages represent only two incidents each. Detailed information is listed in Supplementary Tables S2, S3, S4, and S5.

Province(11 586 cases); Liaoning Province had 117 cases, Shandong Province had 103 cases, and this was, so far, the largest outbreak after the first stage. The total number of infections in Qingdao, Shandong Province, and in other places also exceeded 2 000, with multiple transmission chains and aggregated outbreaks in factories, units, and schools.

We classified the proximal sources of all 285 post-Wuhan domestic incidents: proximal sources in Hubei Province accounted for 78 incidents (27.4%), infections from travelers returning from overseas accounted for 87 (30.5%), imported fomite transmission accounted for 31 (10.9%), virus strains of unknown sources but with overseas genomic lineages accounted for 45 (15.8%), and sources unknown because of unavailable or undeclared data or because of unfinished source investigation information accounted for 44 (15.4%).

4. Discussion

In this study, we categorized all the post-Wuhan outbreaks of COVID-19 infections within mainland China into 285 individual transmission incidents, and those incidents were grouped into four major stages with distinct characteristics. The characteristics of outbreaks are influenced by various factors, including the features of the virus, the responses of governments, and the immunity of the population. Our major goal was to provide a centralized, organized review of all past infections in mainland China. Pinpointing the index patient in a population is difficult when a cluster of infections is investigated retrospectively. Source investigations involved contact tracing from known cases of a cluster, to identify initial interactions with people, objects, and events that were potential sources of the

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infection. Such investigation gradually became routine for response measurements by local centers of disease control and prevention. This process also involves screening the transmission network to identify infections that may be asymptomatic and undiagnosed. Focusing on early infections in a cluster, understanding efficient epidemiological characteristics, and gathering other scientific evidence are critical in determining the proximal source. Given all domestic incidents together, potential sources of incidents were classified into five categories: proximal sources from Hubei Province, infected travelers returning from overseas, imported fomite transmission, sources that were unknown but for which the virus strain was identified as having overseas genomic lineage, and unknown or undeclared sources. Most COVID-19 outbreaks in mainland China after the first stage were caused by imported sources (e.g. infected travelers). Controlling imported infection and transmission is a huge challenge if prevention and control measures are not appropriately followed, domestic transmission will result in large-scale local epidemics.

Vaccines are among the most successful and cost-effective methods of preventing infectious diseases, and COVID-19 is no exception[9]. Since the original SARS-CoV-2 was identified, it has continuously evolved into multiple variants (Alpha, Delta, and Omicron) that have contributed to several pandemic peaks[10–12]. The fourth and fifth stages in mainland China were driven by distinct variants: the fourth (from May to December 2021), by the Delta strain, and the fifth (from December 2021 to March 16, 2022), by the Omicron strain. According to extensive real-world data published in prestigious medical journals, vaccines were less effective against some SARS-CoV-2 variants, and their effectiveness against infection in general waned over time; however, current vaccines, especially booster vaccination, provide good temporary protection against severe disease, hospitalization, and death. Neutralizing antibody responses wane after two doses of inactivated vaccines, but the initial effectiveness of domestic vaccines against the Delta and Omicron variants in China is relatively low[13,14]. A real-world study in Guangzhou in mid-2021 showed that two doses of inactivated vaccines provided only 59.0% protection against infection with the Delta strain, but it prevented severe disease in 100% of recipients. The effectiveness of domestic vaccines against variants requires further evaluation for informing vaccine policy[15]. China's research on messenger RNA vaccine and homologous or heterologous booster vaccination against variants is progressing.

During the first stage of the pandemic, China's government implemented a rapid and sustained containment strategy with innovative technological and organizational approaches that helped contain the outbreaks in three months, despite the lack of effective vaccines and drugs. The first domestic stage ended on April 7, 2020, and the Wuhan lockdown was officially ended the next day; however, viral transmission continued. During the pandemic, many other countries have relied on voluntary public support and cannot enforce stringent public health policies, whereas China has continuously developed and followed the "COVID-zero" strategy that is now called the "dynamic COVID-zero" strategy. Along with the deployment of advanced digital technologies, rapid and cost-effective mass nucleic acid testing is crucial for eliminating potential chains of transmission by identifying asymptomatic infection. For instance, several outbreaks in Beijing were controlled within 28 d by the local government's placement of centralized testing for its entire resident population[16]. Similar responses were also enacted across the nation with variations in details when clusters of local transmission were identified. Apart from massive testing in urgent circumstances, routine testing among high-risk groups and for patients displaying COVID-19-like symptoms is mandatory in hospitals across the nation. These regulations have successfully identified many sporadic cases, preventing potential community transmissions during the early stages.

In Hong Kong, the Omicron BA.2 variant has caused the most devastating stage of infections and deaths, overwhelming the hospitals and fueling a mental health crisis: this surge in infections has been attributed to low levels both of protection by inactivated vaccines and of natural immunity. In China mainland, the percentage of people protected against Omicron infection is less than 30%, which is similar to the corresponding percentage in Hong Kong. According to the data from Hong Kong, if China mainlnd gives up the "dynamic zero-COVID" strategy, an outbreak of COVID-19 of the same magnitude could occur because of the low effectiveness of vaccines against the Omicron variant and the low rates of immunization in the population, and the number of deaths could exceed one million or much worse[17].

The world is experiencing the fourth peak of the COVID-19 pandemic. The Omicron variant is highly contagious, insidious, less symptomatic, and more difficult to detect than the earliest cases in the pandemic, and so the positive cases of the current outbreaks are still on the increase[18]. Adhering to current prevention and control strategies and measures will not only minimize the rates of infections, severe illness, and death but also shrink the areas affected by the disease and its effects on economic and social development. The standards of the global health care community are to protect life first by acting earlier in diseases and tackling problems at their source[19]. This will help restore health care to normal, in which the daily medical needs of the people are the focus.

Regarding when China would ease its COVID policy, on February 15, 2022, Zunyou Wu, Chief Epidemiologist of the Chinese Center for Disease Control and Prevention, declared that several Chinese research teams were investigating more passive measures that differ from both the "zero-COVID" policy and the policies adopted by Western countries; the details of these measures have not yet been developed[20]. Hong Kong has been expected to gradually resume public services in April 2022, and mainland China is likely to take significant action until more vaccination and specific treatment are successfully developed or the variants circulating become milder and no longer pose a public health threat.

This study had several limitations. The information available in public databases was limited, and so our statistical analyses were based on incomplete data. Moreover, 15.4% of the potential sources were unknown because source investigations were unfinished or information was undeclared, which may have caused bias. Lastly, the limited collected data were insufficient for objectively evaluating the effectiveness of control measures. Models do play a significant role in assessing the effectiveness of prevention and control measures.

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Various statistical studies performed in the early stages showed that the early implementation of control measures contributed to reducing reproduction numbers below one implying that timely and rapid control measures have an identifiable large effect on containing the transmission of SARS-CoV-2 virus[21,22]. However, few studies of these measures have been conducted in China, especially in post-Wuhan outbreaks.

To summarize, post-Wuhan COVID-19 outbreaks occurred in four stages in mainland China. Our findings suggest that China has struggled with many major or minor COVID-19 outbreaks since the start of the pandemic in Wuhan, most of which are imported from overseas. Guarding against imported cases and against rebounds in domestic cases remains key for COVID-19 prevention and control, China's policy of "dynamic COVID-zero" is still an effective way to contain the pandemic in the short and mid terms.

Conflict of interest statement

The authors declare that there is no conflict of interest

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Authors' contributions

Guo ZM, Li YF, Guo C discussed the framework of the article. Li YF and Guo C was responsible for manuscript writing. Li YF and Wu Q acquired and analyzed the data. Guo ZM reviewed and edited the content of the whole paper.

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