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Evolution of COVID-19 dynamics in Guangdong Province, China: an endemic-epidemic modeling study

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Abstract

Background From January 2020 to June 2022, strict interventions against COVID-19 were implemented in Guangdong Province, China. However, the evolution of COVID-19 dynamics remained unclear in this period.

Objectives This study aims to investigate the evolution of within- and between-city COVID-19 dynamics in Guangdong, specifically during the implementation of rigorous prevention and control measures. The intent is to glean valuable lessons that can be applied to refine and optimize targeted interventions for future crises.

Methods Data of COVID-19 cases and synchronous interventions from January 2020 to June 2022 in Guangdong Province were collected. The epidemiological characteristics were described, and the effective reproduction number (R_t) was estimated using a sequential Bayesian method. Endemic-epidemic multivariate time-series model was employed to quantitatively analyze the spatiotemporal component values and variations, to identify the evolution of within- and between-city COVID-19 dynamics.

Results The incidence of COVID-19 in Guangdong Province was 12.6/100,000 population (15,989 cases) from January 2020 to June 2022. The R_t predominantly remained below 1 and increased to a peak of 1.39 in Stage 5. As for the evolution of variations during the study period, there were more spatiotemporal components in stage 1 and 5. All components were fewer from Stage 2 to Stage 4. Results from the endemic-epidemic multivariate time-series model revealed a strong follow-up impact from previous infections in Dongguan, Guangzhou and Zhanjiang, with autoregressive components of 0.48, 0.45 and 0.36, respectively. Local risk was relatively high in Yunfu, Shanwei and Shenzhen, with endemic components of 1.17, 1.04 and 0.71, respectively. The impact of the epidemic on the neighboring regions was significant in Zhanjiang, Shenzhen and Zhuhai, with epidemic components of 2.14, 1.92, and 1.89, respectively.

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Conclusion The findings indicate the presence of spatiotemporal variation of COVID-19 in Guangdong Province, even with the implementation of strict interventions. It's significant to prevent transmissions within cities with dense population. Preventing spatial transmissions between cities is necessary when the epidemic is severe. To better cope with future crises, interventions including vaccination, medical resource allocation and coordinated non-pharmaceutical interventions were suggested.

Keywords COVID-19, Spatiotemporal variation, Intervention, Guangdong Province

Text box 1. Contributions to the literature

- This was the first attempt to infer the actual evolution of within- and between-city COVID-19 dynamics in Guangdong Province, China in the period with strict public health interventions.
- A key feature of our study is distinguishing within- and between-city transmission of cases in Guangdong Province that allows us to identify potential strategies for health policy intervention.
- More attention should be paid to the areas with dense population and preventing spatial transmissions when the epidemic situation is severe.

Introduction

Coronavirus disease (COVID-19) is an acute respiratory infection caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which began the global pandemic in March 2020 [1]. As of 25 October 2023, the number of confirmed COVID-19 cases worldwide has exceeded 772 million, with a cumulative death of 6.97 million [2]. WHO comments that the future of COVID-19 remains uncertain [3]. The epidemic and prevention and control mode of COVID-19 needs to be further studied.

From January 2020 to November 2022, a series of intervention measures was implemented against COVID-19 and contained the epidemic. Nevertheless, the epidemic continued to rise one after another, with spatiotemporal variations in prevalence in different regions and stages [4, 5]. However, the epidemic characteristics and spatiotemporal transmission patterns during this period have not been well elucidated yet. Some previous studies explored the patterns of transmission of COVID-19 in time, space and space-time, such as exploring the spatio-temporal features of COVID-19 [6–8], and identifying the determinants of spatiotemporal variations and evolution of dynamics in the epidemic [5, 9, 10]. Furthermore, most studies focused on one or several cities rather than on a finer scale. Up to now, few studies have explored the spatio-temporal variation of COVID-19 in China using the endemic-epidemic multivariate time-series model.

Guangdong Province, located in the shipping hub of the South China Sea, is the largest economic province in China. Due to its geographical and economic advantages and subtropical climate, Guangdong has historically experienced a high incidence of infectious diseases. Some

studies revealed that climate, trade and density of population were important factors of transmission dynamics of COVID-19, reflecting the necessity of studying in Guangdong Province [11–13]. From January 2020 to June 2022, Guangdong launched three levels of emergency responses and policies of normal prevention and control strategy and dynamic zero-COVID strategy against COVID-19. During these stages, it was observed that COVID-19 is heterogeneously distributed in time and space [14, 15]. Analyzing the spatiotemporal dynamic of COVID-19 within and between cities helps further understand the differential effectiveness of strategies at the city/district level and refine interventions.

In this study, we will investigate the epidemiological characteristics and spatiotemporal variation in levels of cities and districts/counties of COVID-19 in Guangdong Province from January 2020 to June 2022. The results can not only infer the component of the spatiotemporal variations in different regions but also reflect the transmission patterns of COVID-19 within and between cities. Moreover, the effect of interventions during different stages would be reflected to optimize public health interventions concretely.

Methods

Data collection

Data of COVID-19 cases reported from January 2020 to June 2022 was used in this study. The data were obtained from the Guangdong Provincial Center for Disease Control and Prevention (GDCDC), concerning the number of reported and confirmed cases of COVID-19 per city and county/district. Geographic data of the administrative interface of each city and district/county in Guangdong were obtained from the Resource and Environmental Science and Data Center [16]. The variables in this study included the effective reproduction number, the effect values of the autoregressive component, the endemic component and the spatiotemporal component.

Information on public health interventions (Table S1) was obtained from official reports. Data on COVID-19 cases and prevention and control measures used in this study can be queried and verified on the official website of the Health Commission of Guangdong Province [17]. The epidemiological characteristics and transmissibility of COVID-19 were described in five stages [18]. The emergency response mechanism is a variety of

emergency plans launched by the government for various public emergencies with the intensity decreasing from level 1 to level 4. Stage 4 was the phase of normalized prevention and control. After that Guangdong entered the phase of the dynamic zero-COVID strategy (Stage 5). Public health interventions were divided into three categories including case-based measures, community measures, and travel-related measures [19].

The effective reproduction number estimated

To describe the transmissibility over time, we estimated the effective reproduction number (R_t) by sequential Bayesian method. R_t was defined as the mean number of secondary infections that were generated by a primary case of infection at time t [20]. If $R_t > 1$ the epidemic will tend to expand, whereas $R_t < 1$ indicates that the epidemic will tend to decline. We used a prior Gamma distribution for the serial interval with a shape parameter (serial interval of 3.4 days) and a scale parameter (standard deviation of 1.2 days) [10, 21, 22].

Endemic-epidemic multivariate time-series models analysis

We adopted the endemic-epidemic model pioneered by Held and colleagues, which has been extensively utilized to explore the transmission dynamics and to gauge the impact of seasonal, sociodemographic, and environmental factors on the spread of various infectious diseases. These include norovirus gastroenteritis, invasive pneumococcal disease, and COVID-19. Several studies have adeptly employed this model to elucidate the nuances of spatiotemporal transmission patterns of COVID-19, shedding light on person-to-person transmission dynamics, seasonal influences, and other contributing factors [23–26]. To determine the variation of spatiotemporal transmission, an endemic-epidemic multivariate time-series model was constructed based on daily data from January 2020 to June 2022.

Endemic-epidemic multivariate time-series model decomposes disease risks into three components, the autoregressive component (reflecting the impact of the past onset of COVID-19 infection on the current outbreak), the endemic component (concerning about long-term trends, seasonal effects, etc.) and the spatiotemporal component (capturing the transmission from other regions) [4, 27–29]. The formula is as follows:

$$\mu_{i,t} = e_{i,t}v_{i,t} + \lambda_{i,t}Y_{i,t-1} + \theta_{i,t} \sum_{i \neq j} [W_{i,j}Y_{i-1,j}] \quad (1)$$

$$\log(\lambda_{i,t}) = \gamma_0 + \gamma_i + \mu_{j,t-1}^T \gamma \quad (2)$$

$$\log(\theta_{i,t}) = \beta_0 + \beta_i + k_{j,t-1}^T \beta \quad (3)$$

$$\log(v_{i,t}) = \alpha_0 + \alpha_i + \beta_t + z_{i,t}^T \alpha + S_{eff} \quad (4)$$

$$S_{eff} = \left\{ \sum_{s=1}^S [K_s \sin(\varphi_s t) + \delta_s \cos(\varphi_s t)] \right\} \quad (5)$$

In Eq.(1), $Y_{i,t}$ denotes the disease counts in region i at time t , which is assumed to follow negative binomial distribution with conditional mean. The choice of this distribution was primarily driven by the variability in susceptibility among COVID-19-affected populations, coupled with the extended duration of the study period. This selection reflects our intention to capture the nuanced dynamics of disease spread over an extended period. $e_{i,t}$ is the offset of region i over time t . In this study, the population density of different regions was added as the offset. $\lambda_{i,t}$, $\theta_{i,t}$ and $v_{i,t}$, denote the autoregressive component, epidemic component and endemic component, and γ_0 , β_0 and α_0 are corresponding intercepts. γ_i , β_i and α_i are the random effects. β and S_{eff} represent the long-term trend and seasonal effect, and $\mu_{j,t}^T$, $k_{j,t}^T$ and $z_{i,t}^T$ denote the covariate matrix of specific component [30, 31]. $W_{i,j}$ is the neighbourhood weights assumed to follow a well-recognized power-law distance decay.

Due to geographical and economic advantages, the epidemic in Guangdong Province is more susceptible to imported cases. Thus this study included imported cases as a covariate incorporated into $\mu_{j,t}^T$, $k_{j,t}^T$ and $z_{i,t}^T$ respectively, and choose the optimal model by Akaike information criteria (AIC). In this study, the power-law method for the endemic-epidemic multivariate time-series model was chosen after comparing AIC of different models (Table S2).

We used R software (version 4.3.1) to produce the graphs and conduct statistical analysis. R package “Epi-Estim” was used to estimate R_t , and “factoextra” was used for cluster analysis. R package “surveillance” was used to construct the endemic-epidemic multivariate time-series models [30].

Result

Epidemiological characteristics

From January 2020 to June 2022, a total of 15,989 COVID-19 cases were reported in Guangdong Province and the incidence rate was 12.6/100,000 population. Of them, 10,483 (65.56%) were imported cases (Table 1). Cases were mainly aged 20 to 59 years. In addition, 8541 (53.42%) cases were positive cases and 7448 (46.58%) were confirmed cases. The population characteristics of the COVID-19 cases varied across different stages. As shown in Table 1, there were no imported cases from abroad in Guangdong during Stage 1. However, there were more imported cases in other stages. The majority

Table 1 Epidemiological characteristics of COVID-19 in Guangdong Province, from January 2020 to June 2022

Stage	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	Overall
Source of infection (Constituent ratio %)						
Local infection	1384 (100.00)	318 (54.64)	13 (0.93)	195 (9.75)	3568 (33.70)	5506 (34.44)
Imported infection	0	264 (45.36)	1392 (99.07)	1806 (90.25)	7021 (66.30)	10,483 (65.56)
Type of cases (Constituent ratio %)						
Positive test cases	67 (4.84)	338 (58.08)	948 (67.47)	1163 (58.12)	6025 (56.90)	8541 (53.42)
Confirmed cases	1317 (95.16)	244 (41.92)	457 (32.53)	838 (41.88)	4564 (43.10)	7448 (46.58)
Age (Incidence rate/10⁵)						
M±SD	46.17±18.03	33.94±13.32	39.06±11.52	39.53±12.91	35.44±15.57	37.18±15.47
0–19	111 (0.37)	60 (0.20)	29 (0.10)	61 (0.20)	1344 (4.47)	1605 (5.33)
20–39	415 (0.91)	345 (0.76)	737 (0.76)	1038 (2.28)	5269 (11.56)	7808 (17.14)
40–59	487 (1.40)	157 (0.45)	593 (1.70)	793 (2.28)	3308 (9.51)	5345 (15.36)
60–79	344 (2.60)	20 (0.15)	45 (0.34)	91 (0.69)	624 (4.71)	1,138 (8.60)
>80	27 (1.16)	0	1 (0.04)	18 (0.77)	44 (1.89)	92 (3.95)
Gender (Incidence rate/10⁵)						
Male	679 (1.01)	370 (0.55)	1092 (1.63)	1500 (2.24)	6558 (9.80)	1,0213 (15.26)
Female	705 (1.17)	212 (0.35)	313 (0.52)	501 (0.84)	4031 (6.73)	5776 (9.64)
Gender ratio	0.96	1.75	3.49	2.99	1.63	1.77
Occupation (Constituent ratio %)						
Occupations at risk	33 (2.38)	6 (1.03)	95 (6.76)	179 (8.95)	1099 (10.38)	1376 (8.83)
Occupations of key institutions and places	300 (21.68)	252 (43.30)	769 (54.73)	922 (46.08)	3782 (35.72)	5879 (37.71)
Other occupations	1051 (75.94)	324 (55.67)	541 (38.51)	900 (44.98)	5708 (53.90)	8334 (53.46)
Total (Incidence rate/10⁵)	1384 (1.09)	582 (0.46)	1405 (1.11)	2001 (1.58)	10,589 (8.35)	15,989 (12.6)

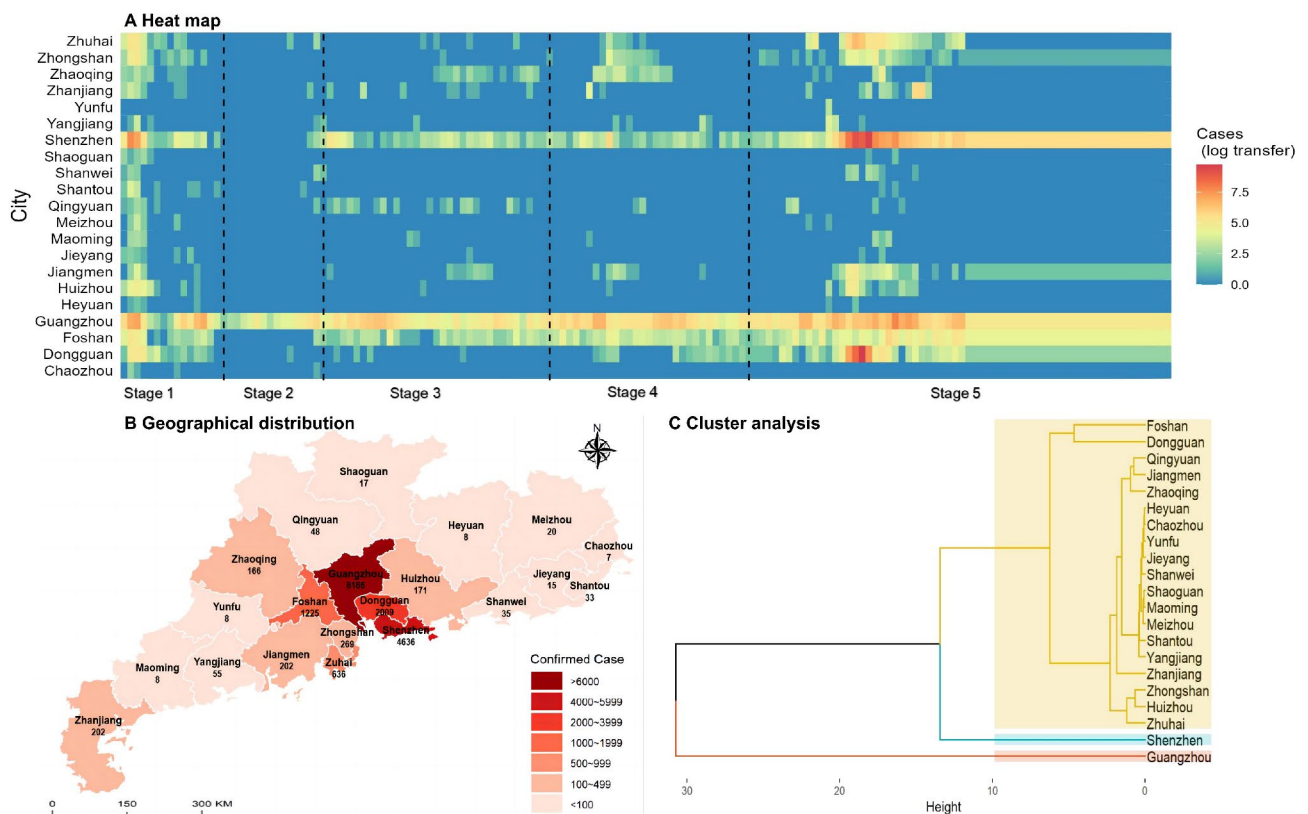


Fig. 1 Heat map, geographical distribution and cluster analysis of COVID-19 cases in Guangdong Province, from January 2020 to June 2022

of cases were aged 40–59 years in Stage 1, while the majority of cases were aged 20–39 years in other stages.

We created heat maps (Fig. 1A) for each city in each stage. Overall, the growth process of cases in all cities was similar, showing the evolution characteristics of “explosive growth and followed by a slow decline”. Figure 1 also revealed that the COVID-19 cases in Guangdong were mainly distributed in the PRD including Guangzhou (6166 cases), Shenzhen (4636 cases), Foshan(1225 cases) and Dongguan(2009 cases). This feature of geographical distribution is more obvious in Stage 1 and Stage 5.

The clusters analysis identified four clusters including Guangzhou, Shenzhen, Foshan and Dongguan, and other cities. Guangzhou, the capital of Guangdong Province, accounted for 38.56% of all cases. Shenzhen (4636 cases) accounted for 28.99% of the cases. The cluster covering two cities, Dongguan (2009 cases) and Foshan (1225 cases), contributed to 20.23% of the cases. The cluster which covered other cities accounted for 12.21% of cases.

Interventions and temporal transmissibility of five stages

Figure 2 shows the temporal distribution and interventions from January 2020 to June 2022. In Stage 1, interventions were implemented such as screening and quarantine in high-risk groups, tracing and management for close contact, and strict community health management. In Stage 2, residents who come from or have a history of travel to overseas countries and territories should be quarantined for 14 days and health management should be carried out [32]. Resumption of enterprises and

dine-in services were allowed in low-risk areas [33]. In Stage 3, strict travel management was continued [34] and vaccination was fully launched for key population groups [35]. In Stage 4, a vaccination campaign against COVID-19 among people over the age of 12 was launched [36]. In Stage 5, the surveillance mode of “antigen screening+nucleic acid diagnosis” was implemented. Detailed interventions are illustrated in Fig. 2 and Table S1.

Most cases were distributed in 2020 and 2022 while fewer cases in 2021. The peaks of the epidemic were observed in Stage 1 (1384 cases) and Stage 5 (10,589 cases). From Stage 2 to Stage 4, with the implementation of prevention and control measures, the number of cases decreased and the effective reproduction number (R_t) remained around the critical threshold of 1. In Stage 5, the number of cases was higher than the previous periods. After the Omicron variant appeared in Guangdong Province on December 16, 2021, the number of cases (312 cases) reached its peak in the two years of epidemic prevention and control in Guangdong despite the adoption of a dynamic zero-COVID strategy. The number of cases was higher than that in the previous period when the original strains or Delta variant were the main epidemic variants. The estimated R_t increased significantly in February 2022 with the highest value (1.39, 95% confidence interval [CI]: 1.32, 1.46), subsequently declined to less than 1 about one month later. These results reflected the effectiveness of specific measures and helped to provide targeted optimization method.

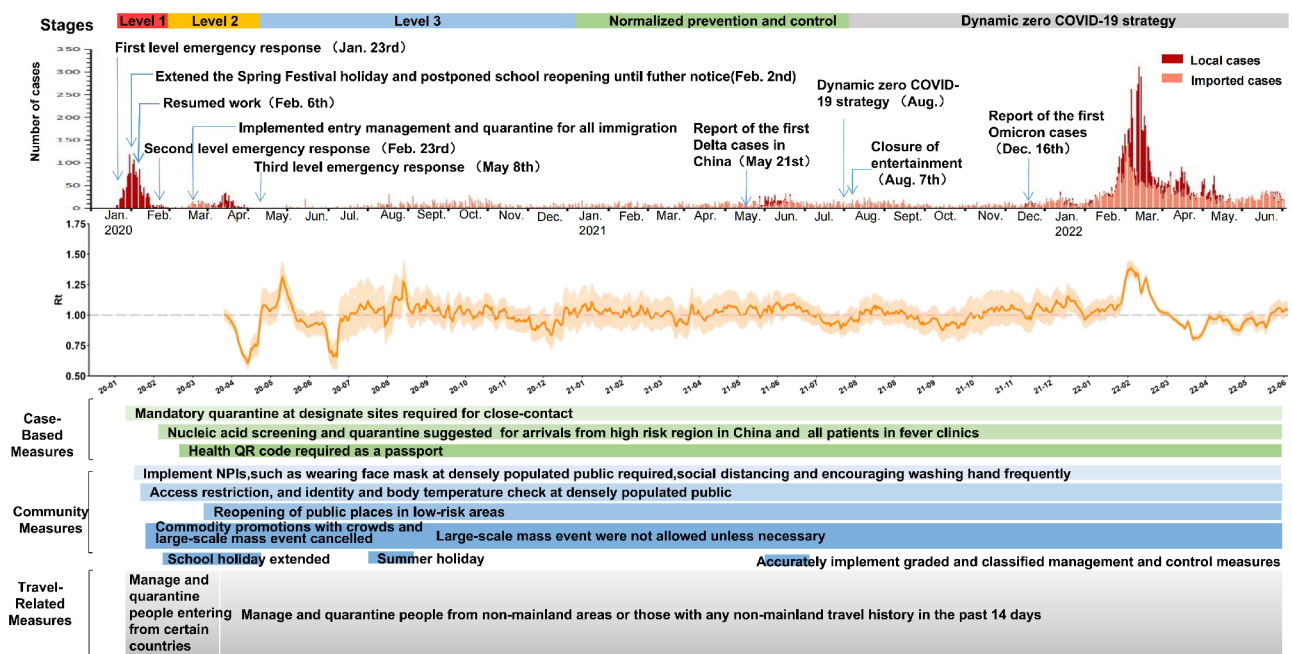


Fig. 2 The epidemic curve, reproduction number (R_t) and public health interventions of COVID-19 in Guangdong Province, from January 2020 to June 2022

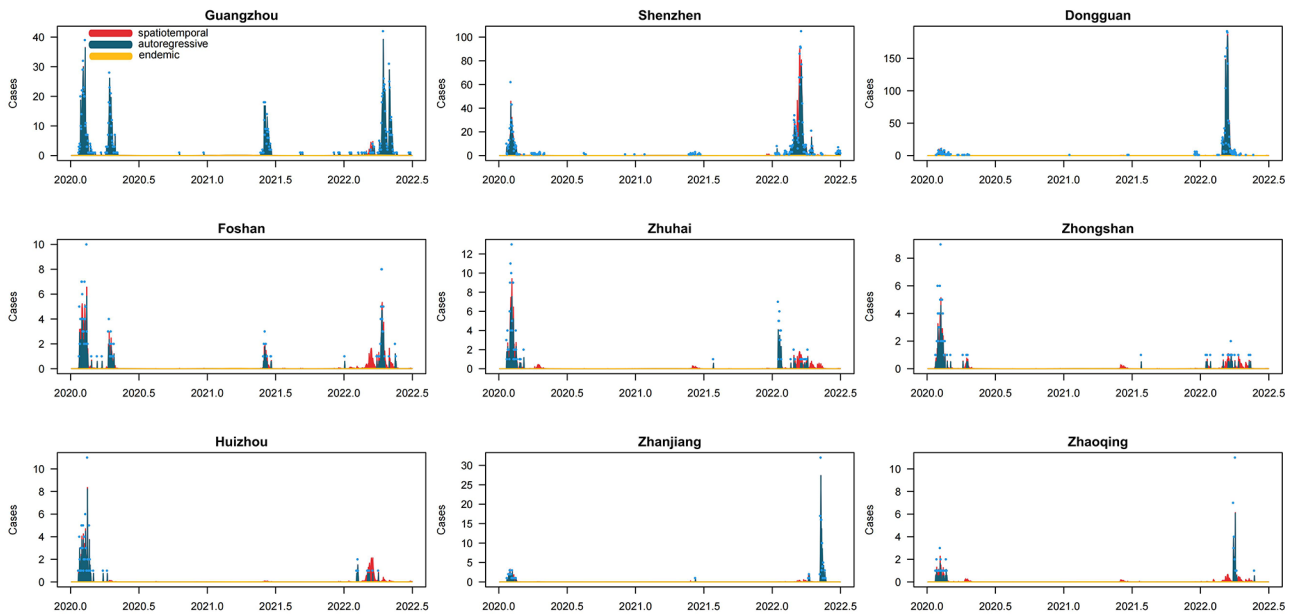


Fig. 3 Fitted components in the endemic-epidemic multivariate time-series model for the selected six cities in Guangdong Province from January 2020 to June 2022

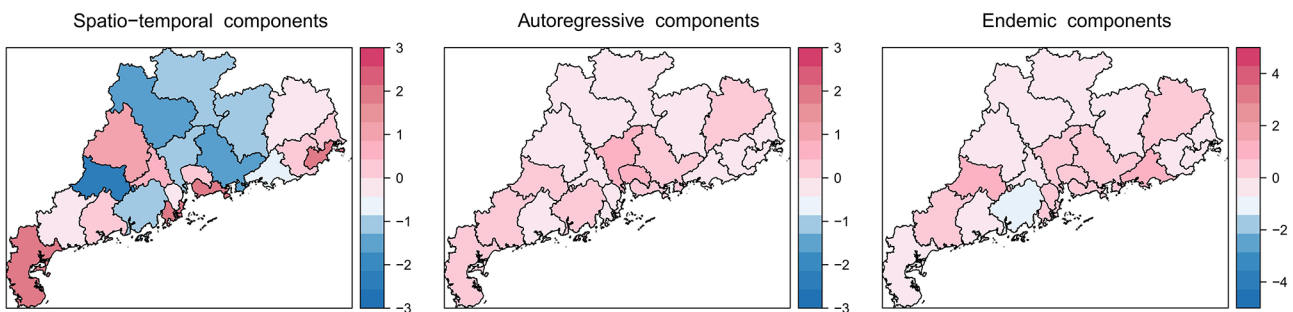


Fig. 4 Maps of the estimated random intercept at the city level based on the endemic-epidemic multivariate time-series model in Guangdong Province from January 2020 to June 2022

Spatiotemporal variation

Power-law method for the endemic-epidemic multivariate time-series model, which included imported cases as a covariate incorporated into the endemic component, was chosen due to the lowest value of AIC (6875.416) (Table S2). The total effect values of the autoregressive component and the spatiotemporal component were 0.804 (95%CI: 0.756, 0.852) and 0.089 (95%CI: 0.080, 0.097). The endemic component was 0.010, (95%CI: 0.006, 0.015) and the estimated value of imported cases was 0.453, (95%CI: 0.403, 0.503). This suggested that the incidence of COVID-19 in Guangdong Province was mainly influenced by the autoregressive component. Transmission risks within cities were higher than the risks between cities.

The follow-up impact from previous infections appeared strong in Dongguan, Guangzhou and Zhanjiang, with the autoregressive component as 0.48, 0.45, 0.36, respectively. The local risk seemed high in Yunfu,

Shanwei and Shenzhen, with the endemic component as 1.17, 1.04 and 0.71, respectively. The impact of the epidemic on the neighboring regions was large in Zhanjiang, Shenzhen and Zhuhai, with the epidemic component as 2.14, 1.92, and 1.89, respectively.

Figure 3 displays the relative contributions of the three components in driving the incidence of COVID-19 among the high-incidence regions (total reported cases > 50). The high-incidence areas, including Zhanjiang, Zhaoqing, Guangzhou, Foshan, Zhongshan, Zhuhai, Dongguan, Huizhou and Shenzhen, had lots of autoregressive components, indicating that these were predominantly influenced by the previous infection in their regions. Few endemic distributions in these cities reflected low risks of local transmission. Foshan, Zhuhai, Shenzhen and Huizhou had more spatiotemporal components in Stage 1 and 5, thus these cities may suffer infection of COVID-19 from neighboring cities in these phases. Concretely, the districts/counties of Longgang,

Xiangzhou, Chancheng, Nanhai, and Huicheng had quite a few components of spatiotemporal incidence in the same stages. (Fig. S2).

As shown in Fig. 4, a low random effect of the autoregression was observed in high-incidence regions. What's more, the random intercepts exhibited variation between cities in the spatiotemporal component. Southern and central Guangdong including Zhanjiang, Zhuhai, Shenzhen and Foshan, displayed a relatively high spatio-temporal incidence (Fig. S3).

Discussion

In this study, the epidemic characteristics, spatiotemporal variation and association of COVID-19 transmission were systematically analyzed based on the anti-COVID-19 processes and practical data from January 2020 to June 2022 in Guangdong Province. We found that significant spatial variation was observed in the spatiotemporal component. Most regions had vast autoregressive components and few endemic and spatiotemporal components. This study inferred the spatiotemporal transmission patterns of COVID-19 and provided targeted suggestions for future crises.

During the study period, the cases were mainly imported cases (65.56%), and the infections were mainly distributed in the PRD. The reason could be associated with trade networks and population density. Guangdong Province is one of the largest economic provinces with a large migrant population leading to high risks of epidemic importation [37]. The Pearl River Delta is one of the main regions of China to participate in economic globalization. It has formed a relatively developed economy and transportation network with Guangzhou and Shenzhen as the center, connecting Hong Kong and Macao and connecting the whole province and the country. Thereby there were more people and frequent activities in PRD contribute to the high risk of infection [38, 39]. Our findings align with previous studies, which have consistently demonstrated that cases of COVID-19 are mostly observed in regions with dense populations and frequent activities of trade [40, 41].

We observed that the epidemic curve and transmissibility of COVID-19 declined in time due to strict and timely interventions. From January 2020 to June 2022, the epidemic curve was flatter for most of the time and the transmissibility remained low, as reflected by R_t . During the periods of more severe situations such as Stage 1 and Stage 5, stricter strategies of a level 1 emergency response and the dynamic zero-COVID strategy were timely taken. In May 2021, the SARS-CoV-2 Delta variant first appeared in Guangdong, China and contributed to the local epidemic in Guangzhou and Shenzhen [14, 42]. In December 2021, the Omicron virus first appeared in Guangdong demonstrating a higher transmission rate

than the Delta variant, resulting in a broader spread and increased infections [43]. However, the epidemic was successfully controlled proving the effectiveness of strict and timely strategies.

We found that significant spatial variation was observed in the spatiotemporal component across the cities and districts, while the autoregressive and endemic components were more spatially homogeneous during the period of implementing strict interventions. Most regions had vast autoregressive components and few endemic and spatiotemporal components. The pronounced autoregressive component underscored the significant within-city transmission risks, which are closely tied to the population density in Guangdong province. This serves as a stark reminder that even amidst stringent interventions, the threat of COVID-19 transmission in densely populated cities persists. It underscores the necessity for continuous interventions, particularly those aimed at bolstering public awareness around personal hygiene practices and the importance of vaccination. Such measures are critical for mitigating the risk of local infections in areas with high population density. Our results were different from the results of studies in settings without rigorous interventions which showed more endemic and spatiotemporal components [23]. This may be due to the influence of strict interventionist and policies. The low risks of local and trans-regional transmission may be because of the active surveillance and travel-related measures adopted in Guangdong [44, 45]. As for the evolution of variations during the study period, there were more spatiotemporal components in several cities, including Zhanjiang, Foshan, Zhuhai, Shenzhen and Huizhou in stage 1 and 5. All components were fewer from Stage 2 to Stage 4. These suggested that even if strict measures were taken, more attention should be paid to preventing spatial transmissions in these areas when the epidemic situation is severe. Simultaneous and coordinated interventions in multiple areas were recommended, to prevent being infected by neighboring regions [46]. Specifically, the implementation of non-pharmaceutical interventions such as restrictions on movement, border measures, and quarantine of travelers arriving from affected areas was necessary [37, 47].

Some limitations of this study should be acknowledged. Firstly, the cases were recorded in the reported address, which may result in inconsistencies with the real location where they were infected. Secondly, the risk of imported infection and local epidemic varies owing to the differences in socio-economic circumstances, climate and geography [48]. Our study focused on the spread of COVID - 19 during strict interventions, selecting variables directly related to these measures. Although we acknowledged the importance of socio - economic and environmental factors, their inclusion was restricted

due to the availability of data and the simplicity of the model. Future research aims to address these limitations for a more thorough understanding. Thirdly, China has managed COVID-19 with measures against Class B infectious diseases, instead of Class A infectious diseases, in a major shift of its epidemic response policies since January 8, 2023. This may influence the transmission of COVID-19 and implementation of interventions, posing challenges to the applicability and uniformity of our research conclusions. However, our findings remain pertinent. While policy revisions may diminish the focus on particular severe interventions, the targeted and coordinated interventions we emphasized align with the requirement of the current policies for flexible public health strategies. Our research offers insights into the development of new strategies and lays the groundwork for future research. Future studies should build upon our findings to further explore how policy changes affect the transmission patterns of COVID-19 and the efficacy of public health measures.

Conclusions

This study clarified the evolution of within- and between-city COVID-19 dynamics in Guangdong and provided lessons and recommendations of specific measures against future pandemic threats of COVID-19. In the context of implementing strict interventions, the spatio-temporal variation of COVID-19 still existed in Guangdong Province. It is necessary to prevent the transmission within cities in the areas with dense population. More attention should be paid to preventing spatial transmissions between cities in Guangdong when the epidemic situation is severe. In addition, in order to better cope with future crises, interventions including vaccination, enhanced public health education and coordinated non-pharmaceutical interventions were suggested.

Abbreviations

AIC	Akaike information criteria
CI	Confidence interval
COVID-19	Corona Virus Disease 2019
PRD	Pearl River Delta region

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13690-024-01406-1>.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Supplementary Material 5

Author contributions

ZH and LL (Liling Lin) performed the statistical analysis and wrote the manuscript. LL (Lifeng Lin) and JX conceived the study idea and designed the study. XL, ZR, JH, JZ, LZ, DG, JX, WZ and ZZ contributed to data visualization. YL (Yan Li), YH and YL (Yihong Li) collected data and verified the underlying data. WZ and YH verified the manuscript. All authors contributed to the article and approved the submitted version.

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Data availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the ethics committee of Guangdong Provincial Center for Disease Control and Prevention (No. W96-027E-202104).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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